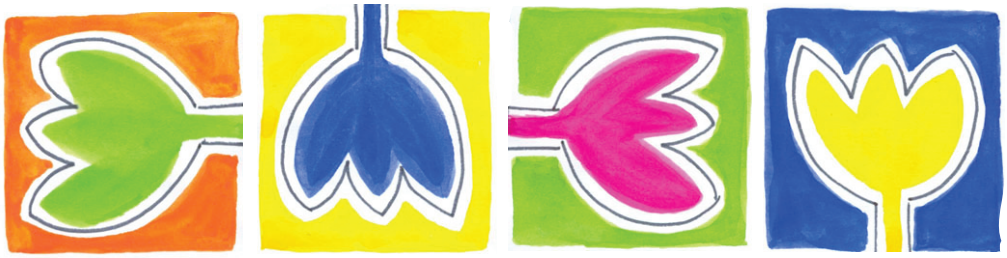
swiss childhood cancer registry



annual report 2011-2012

Swiss Childhood Cancer Registry

Annual Report 2011/2012

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Logo: Elsbeth Kuehni

Bern, Swiss Childhood Cancer Registry

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1. Introduction

The Swiss Childhood Cancer Registry (SCCR) is the national population-based cancer registry for children and adolescents in Switzerland. New cancer diagnoses, clinical information, details on treatment and long-term follow-up (survival, second primary neoplasms and late effects) have been registered in the SCCR since 1976. With many associated research projects and through close collaboration with clinicians it contributes to understanding the causes of cancer in children, improving follow-up care and reducing late effects.

The SCCR is located at the Institute of Social and Preventive Medicine (ISPM) at the University of Bern. It is operated jointly by the Swiss Paediatric Oncology Group (SPOG) and the University of Bern. All Swiss paediatric haematology-oncology centres report newly diagnosed cases to the registry and send annual updates on clinical follow-up. The SCCR began to systematically collect data from other sources in 2007, including the cantonal cancer registries, other hospitals, pathology laboratories and the Swiss Federal Statistical Office (SFSO). As of 31 December 2011, data from 8712 patients have been registered.

The SCCR is authorized to collect non-anonymised data by the Federal Commission of Experts for Professional Secrecy in Medical Research (Eidgenössische Expertenkommission für das Berufsgeheimnis in der medizinischen Forschung).

The SCCR is an associated member of the National Institute for Cancer Epidemiology and Registration (NICER), of the European Network of Cancer Registries (ENCR) and of the International Association of Cancer Registries (IACR), and collaborates with childhood cancer registries throughout Europe.

This fifth annual report covers the routine analyses of all children diagnosed between 1 January 1976, and 31 December 2011. Activities and projects of the SCCR are described for the years 2011 and 2012. This report contains:

- An overview of the organisation and team of the SCCR, SPOG and the participating paediatric haematology-oncology centres (**Chapter 2**)
- A summary of the data collected in the registry up to 31 December 2011 (**Chapter 3**)
- A list of current research projects of the SCCR (**Chapter 4**)
- A list of publications (**Chapter 5**)
- Abbreviations and appendix (**Chapters 6 & 7**)

Our website (www.childhoodcancerregistry.ch) contains further information, including past annual reports and scientific publications.

We would like to thank all the children and their families, and all adolescent and adult childhood cancer survivors, for allowing us to collect their data. We also thank the physicians and data managers of the Swiss Paediatric Oncology Group for their excellent collaboration. Our thanks also go to the cantonal cancer registries, the National Institute for Cancer Epidemiology and Registration (NICER), the Swiss Federal Statistical Office (SFSO), the Federal Office of Public Health (FOPH) and the pathology laboratories for their cooperation. Finally, we thank our supporters for their generous contributions.

2. Organisation of the Swiss Childhood Cancer Registry

The Swiss Childhood Cancer Registry (SCCR) is a member of the Swiss Paediatric Oncology Group (SPOG) and is organised as a joint operation of the Institute of Social and Preventive Medicine (ISPM) at the University of Bern and the SPOG.

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Bern (Universitätsklinik für Kinderheilkunde, Inselspital)	K. Leibundgut, Prof MD	F. Julmy N. Beusch
Genève (Hôpital des Enfants, Hôpitaux Universitaires de Genève [HUG])	M. Ansari, MD	G. Perrenoud, MSc
Lausanne (Service de Pédiatrie, Centre Hospitalier Universitaire Vaudois [CHUV])	M. Beck Popovic, PD MD	R.-E. Garcia, MD
Bellinzona (Reparto di Pediatria, Ospedale S. Giovanni, Bellinzona)	P. Brazzola, MD	P. Brazzola, MD
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2.3 General information

Aims

The Swiss Childhood Cancer Registry collects information on the diagnosis, treatment and follow-up of cancer in children and adolescents in Switzerland and provides data for national and international statistics and research projects:

- To collect representative, population-based data on cancer in children and adolescents in Switzerland (cancer incidence, prevalence, time trends, regional distribution and survival rates).
- To document diagnostic evaluations, treatment and participation in clinical trials.
- To describe short term and long term prognosis (mortality, morbidity and quality of life) after cancer in childhood and adolescence – (remission, relapses, survival, late effects and quality of life).
- To provide a research platform for clinical, epidemiological and basic research

It thus contributes to:

- Continuous improvement of treatment
- The planning of health services
- Identifying possible late effects of therapy, with the aim to diagnose and treat them early and prevent them in future
- Research into the aetiology of cancer in children and adolescents.

Inclusion criteria

The SCCR registers all children and adolescents aged 0 to 20 years resident, or treated in Switzerland, diagnosed with:

- Acute and chronic leukaemias, including myelodysplastic syndrome
- Lymphomas
- Malignant solid tumours
- Central nervous system tumours (CNS), malignant and benign tumours
- Langerhans cell histiocytosis (LCH)

Children and adolescents who are not Swiss residents but are diagnosed or treated in Switzerland are registered, but they are excluded from analyses of incidence and survival.

Sources of data

Data on children and adolescents with cancer are collected from several sources, including:

- The nine Swiss centres for paediatric oncology and haematology (**Chapter 2.2**)
- Other hospitals
- Clinical and epidemiological registries (e.g. brain tumour registry, bone tumour registry, Swiss growth registry etc.)
- Cantonal cancer registries, organised in the National Institute for Cancer Epidemiology and Registration (NICER)
- The Swiss Federal Statistical Office (SFSO; Swiss mortality statistics)
- Pathology laboratories

Most children (95%) are reported by one of the nine Swiss centres for paediatric oncology and haematology. Local data managers complete forms for all newly diagnosed patients. Basic information on diagnosis is later completed with information on treatments, remissions, relapses, transplantations and late outcomes. These forms are sent to the SCCR and information is entered into the database. Important medical documents (e.g. pathology reports) are scanned and stored electronically using a pseudonym. Paper copies are destroyed. Information on Swiss residency is validated through municipal population registers.

Data on follow-up care in paediatric oncology and haematology centre is extracted annually from patients' hospital records for the first five to ten years after diagnosis (page 18, **Chapter 3.2**). To assess outcomes after the children have left the clinic, patients are directly contacted with a questionnaire (**Chapter 4**: Swiss Childhood Cancer Survivor Study and Follow-up care after childhood and young adult cancer) and data is linked to mortality records (SFSO) and to records from cantonal cancer registries (**Chapter 4:** Mortality and second primary cancers after cancer in childhood and adolescence). For children not treated in a paediatric oncology and haematology centre, clinical follow-up from hospitals is often not available, but long-term epidemiological follow-up is done via questionnaires and by assessment of second primary neoplasms and mortality as for the other patients (page 18, **Chapter 3.2**).

Clinical database

The current SCCR database was set up in 2007. The following information is collected:

- Tumour diagnosis, date of diagnosis, morphology, topography, stage, metastases
- Other diagnoses (relevant pre-existing conditions)
- Relevant laboratory and clinical data
- Treatment (clinical trial participation, chemotherapy, radiotherapy, surgical intervention, bone marrow transplantation) and treatment centres involved
- Follow-up data (changes of treatment, remissions, relapses, survival/death and cause of death)
- Late adverse outcomes (e.g. cardiovascular diseases, second primary neoplasms and endocrine disorders)

Trust centre

Since 2010, personal information (name and address) is stored in a separate database in the trust centre. The trust centre validates addresses, residence status, nationality, and vital status via municipal population registers. This personal information is strictly separated from clinical information contained in the SCCR database. The following data is collected:

- Patient names, address at time of diagnosis, address history and current address
- Date of birth, sex, first language
- Residency and nationality at time of diagnosis
- Vital status and date of death
- Parental professions, parental dates of birth

Tumour coding

All tumours are coded according to the following international classification systems (see appendix):

- International Classification of Childhood Cancer, third edition (ICCC-3)[1]
- International Classification of Diseases for Oncology, third edition (ICD-O-3)[2]
- International Classification of Diseases and Related Health Problems, tenth revision (ICD-10)[3]

In the annual report, the main diagnostic groups of the ICCC-3 are used:

I. Leukaemias, myeloproliferative diseases, and myelodysplastic diseases

II. Lymphomas and reticuloendothelial neoplasms

III. CNS and miscellaneous intracranial and intraspinal neoplasms

IV. Neuroblastoma and other peripheral nervous cell tumours

V. Retinoblastoma

VI. Renal tumours

VII. Hepatic tumours

VIII. Malignant bone tumours

IX. Soft tissue and other extraosseous sarcomas

X. Germ cell tumours, trophoblastic tumours, and neoplasms of gonads

XI. Other malignant epithelial neoplasms and malignant melanomas

XII. Other specified and unspecified malignant neoplasms

Langerhans cell histiocytosis (LCH), which is not included in ICCC-3, is reported separately.

1 Steliarova-Foucher E, Stiller C, Lacour B, Kaatsch P. International Classification of Childhood Cancer, Third Edition. Cancer 2005; 103:1457-1467.

2 World Health Organization. International Statistical Classification of Diseases for Oncology - Third Edition (ICD-O-3). Geneva: World Health Organization; 2000.

3 World Health Organization. International Statistical Classification of Diseases and Related Health Problems - Tenth Revision. Geneva: World Health Organization; 1993.

Data protection

In 2004, the SCCR received a special authorization (Sonderbewilligung) from the Swiss Federal Commission of Experts for Professional Secrecy in Medical Research. In June 2007, this was followed by a general authorization (Registerbewilligung) permitting collection of cancer data from children and adolescents throughout Switzerland by obtaining written, oral or silent consent. A copy of the document provided by the expert commission can be downloaded from our homepage,[4] together with explanations in French and German. At time of diagnosis, all patients and their parents are informed about the childhood cancer registry by the treating physician. The families have the right to prevent transfer of non-anonymised data to the registry (veto power/possibility to opt out). Records of these patients are fully anonymised. Patients are also informed about the registry in hospital brochures, on hospital notice boards, and by patient organisations. All data in the SCCR is kept strictly confidential. Personal information (names, addresses) is stored in a separate database (Trust centre), separated from clinical information.

Data protection measures of the SCCR were examined by the Federal Data Protection and Information Commissioner and the cantonal data protection officer of Bern in 2010. In collaboration with these authorities, data collection and data storage modalities were revised and refined. The new procedures were approved by the Federal Commission of Experts for Professional Secrecy in Medical Research in 2010.

4 http://www.childhoodcancerregistry.ch/index.php?id=2451

Funding

The SCCR thanks the following supporters for their financial contributions towards daily running and continuous development of the registry. Supporters of scientific research projects are listed in **Table 7**, page 30.

Main fund givers 2011/2012

- Schweizerische Konferenz der kantonalen Gesundheitsdirektoren und –direktorinnen (GDK)
- Kinderkrebshilfe Schweiz
- Schweizerische Pädiatrische Onkologie Gruppe (SPOG)
- Stiftung für krebskranke Kinder Regio Basiliensis
- Interpharma AG
- AXA-Winterthur

Other fund givers 2011/2012

- Novartis
- GlaxoSmithKline
- Takeda Pharma
- Celgene
- CSL Behring
- Bayer AG Schweiz
- Prosperita, Stiftung für berufliche Vorsorge

3. Routine Analyses

Overview

The SCCR registers all tumours diagnosed and treated in Switzerland, classified according to the ICCC-3 and Langerhans cell histiocytosis (LCH) in patients aged 0 to 20 years at time of diagnosis. This annual report covers the time period from 1 January 1976 until 31 December 2011. To calculate incidence we count the number of primary neoplasms (cases), which is slightly higher than the number of patients. Patients with more than one primary tumour diagnosed before age 20 years are counted separately for each new tumour.

The section on routine analyses includes three chapters:

Chapter 3.1 presents data on all cases registered in the SCCR. This includes cases resident in Switzerland or abroad, who are diagnosed or treated in Switzerland.

Chapter 3.2 presents data on cases resident in Switzerland, aged 0 to 14 years at diagnosis. This is the age group usually covered in international publications, therefore tables and figures can be directly compared with data from other countries. Registration in Switzerland is more than 95% complete for this age range, allowing calculation of incidence and survival.

Chapter 3.3 presents data on cases resident in Switzerland, aged 15 to 20 years at diagnosis. The SCCR is striving to improve completeness for this age group and is now presenting an overview table. Patients of this age group are treated in a large number and variety of clinics and therefore registration is less complete. Data comparison with cantonal cancer registries has improved completeness of data on adolescents for cantons with a cancer registry. Nevertheless, cancer registration in adolescents remains incomplete in the SCCR and is not population based.

3.1 All cases registered in the SCCR (N=8712)

This chapter describes data from all cases diagnosed 1976-2011, resident in Switzerland or abroad, diagnosed or treated in Switzerland (N=8712).

Up to 31 December 2011, a total of 8712 cases classifiable according to the ICCC-3, or Langerhans cell histiocytosis (LCH), have been registered in the SCCR. These tumours were diagnosed in 8608 patients. Among these, 8506 patients had only one primary neoplasm, 100 patients had two primary neoplasms and 2 patients had three primary neoplasms at age 0-20.

The SCCR started in 1976. Initially, it registered only patients aged 0 to 15 years who participated in clinical trials. Non-trial patients have been included since 1981, resulting in a significant increase in registered cases. In the early 1990s, the introduction of the first electronic database further increased case registration. Since then, annual registration has remained stable (**Figure 1, Table 1**). In the last five years (2007-2011), a total of 1266 newly diagnosed cases were registered; among them 1139 in Swiss residents.

Swiss residents account for 7728 (89%) of all cases and foreign residents for 984 (11%) cases (**Table 2**). Fifty-eight per cent (118/344) of retinoblastoma patients were foreign residents. This is due to the outstanding national and international reputation of the Jules Gonin Hospital in Lausanne, which is the national centre for retinoblastoma treatment but also attracts many patients from abroad.

Figure 1 – Annual number of registered cases over time

Swiss and foreign residents, age at diagnosis 0-14 years; period of diagnosis 1976-2011; all diagnoses (ICCC-3 or Langerhans cell histiocytosis); N=6701

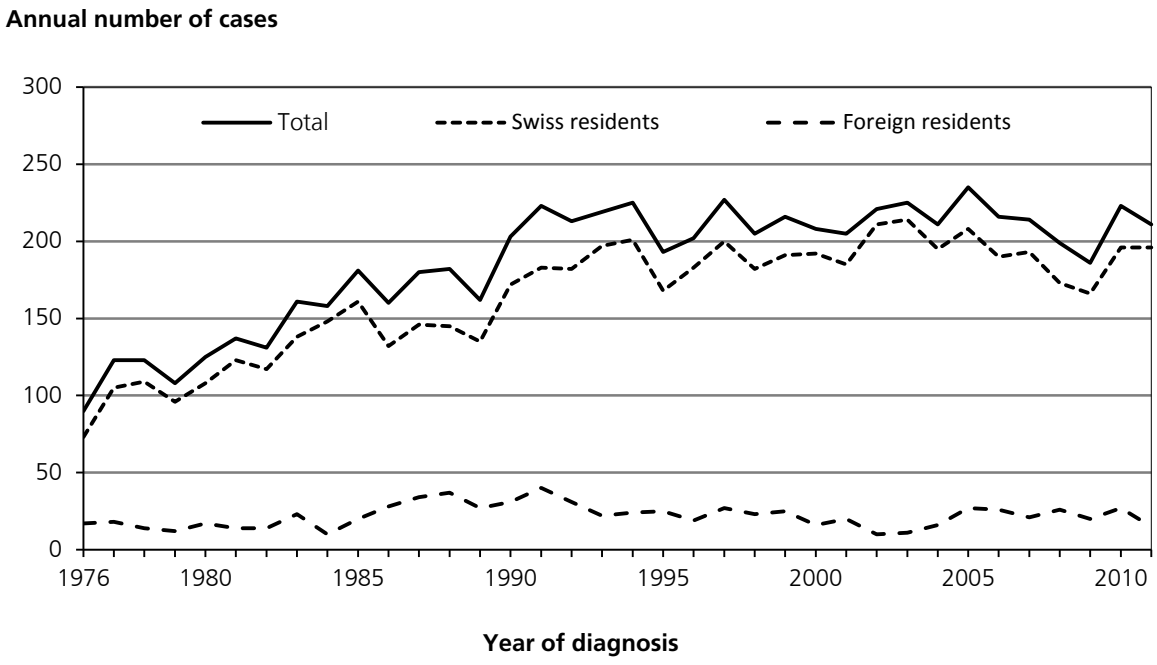


Table 1 – Total number of cases registered, by period of diagnosis

Swiss and foreign residents, age at diagnosis 0-20 years; period of diagnosis 1976-2011; all diagnoses (ICCC-3 or Langerhans cell histiocytosis); N=8712

	All patients Age at diagnosis (years)		**Swiss residents** Age at diagnosis (years)		**Foreign residents** Age at diagnosis (years)	
Year of diagnosis	0-14	15-20	0-14	15-20	0-14	15-20
1976-1981*	706	187	614	167	92	20
1982-1986	791	248	696	223	95	25
1987-1991	950	290	781	263	169	27
1992-1996	1052	327	931	278	121	49
1997-2001	1061	341	950	315	111	26
2002-2006	1108	385	1018	353	90	32
2007-2011	1033	233	923	216	110	17
	6701	**2011**	**5913**	**1815**	**788**	**196**

* This period includes 6 years instead of 5.

Table 2 - Total number of cases registered, by country of residence

Swiss and foreign residents, age at diagnosis 0-20 years; period of diagnosis 1976-2011; all diagnoses (ICCC-3 or Langerhans cell histiocytosis); N=8712

			Age at diagnosis (years)			
	Total		0-14		15-20	
Country of residence	n	%	n	%	n	%
1 Switzerland	7729	88.7	5913	88.3	1815	90.3
2 Foreign countries	983	11.3	787	11.7	196	9.7
a Europe	617	7.1	519	7.7	112	5.6
Neighbouring countries	*383*	*4.4*	*314*	*4.7*	*69*	*3.4*
Austria	*13*	*0.1*	*11*	*0.2*	*2*	*0.0*
France	*126*	*1.4*	*91*	*1.4*	*35*	*1.5*
Germany	*69*	*0.7*	*65*	*1.0*	*4*	*0.0*
Italy	*155*	*1.8*	*129*	*1.9*	*26*	*1.3*
Liechtenstein	*20*	*0.2*	*18*	*0.3*	*2*	*0.0*
Other European countries	*234*	*2.7*	*205*	*3.1*	*43*	*2.13*
b Middle East	46	0.5	23	0.3	9	0.4
c North Africa	159	1.8	121	1.8	38	1.9
d Other African countries	41	0.5	31	0.5	10	0.5
e Other countries	120	1.4	94	1.4	27	1.3
TOTAL	**8712**	**100.0**	**6701**	**100.0**	**2011**	**100.0**

3.2 Swiss residents aged 0-14 years at diagnosis (N=5913)

This chapter relates only to cases aged 0-14 years and resident in Switzerland at diagnosis with a tumour coded according to ICCC-3 or a Langerhans cell histiocytosis. This age group is usually covered by international publications; tables and figures can be compared directly to data from other countries. By 31 December 2011, the SCCR contained data of 5913 tumours diagnosed in this population.

Diagnoses

The International Classification of Childhood Cancer (ICCC-3) distinguishes 12 groups of cancers (**Table 3**). The most common are leukaemias (33% of all cancers), followed by tumours of the central nervous system (20%; especially brain tumours); and lymphomas (13%). Other cancers arise from embryonic tissue. These include neuroblastoma (7%) from primitive neural tissue, nephroblastoma (5%) from renal tissue, hepatoblastoma (1%) in the liver, retinoblastoma (3%) from cells of the retina, as well as germ cell tumours (3%). The latter may arise in the gonads (ovaries and testes), or in other sites, for example in the brain (intracranial germ cell tumours). In older children, malignant bone tumours (4%) and soft tissue sarcomas (7%), which arise from abnormal connective tissue, are occurring with increasing frequency. Sometimes children also develop melanomas and other rare tumours (3%). An intermediate position is hold by Langerhans cell histiocytosis (3%), which is not officially counted as malignant disease. But since they are treated similarly to cancer and in rare cases also may result in death, they are recorded in the Swiss Childhood Cancer Registry. The relative frequency of the different tumours varies significantly with age (**Table 3** and **Figure 2**).

Table 3 – Main diagnostic groups according to ICCC-3, by age at diagnosis

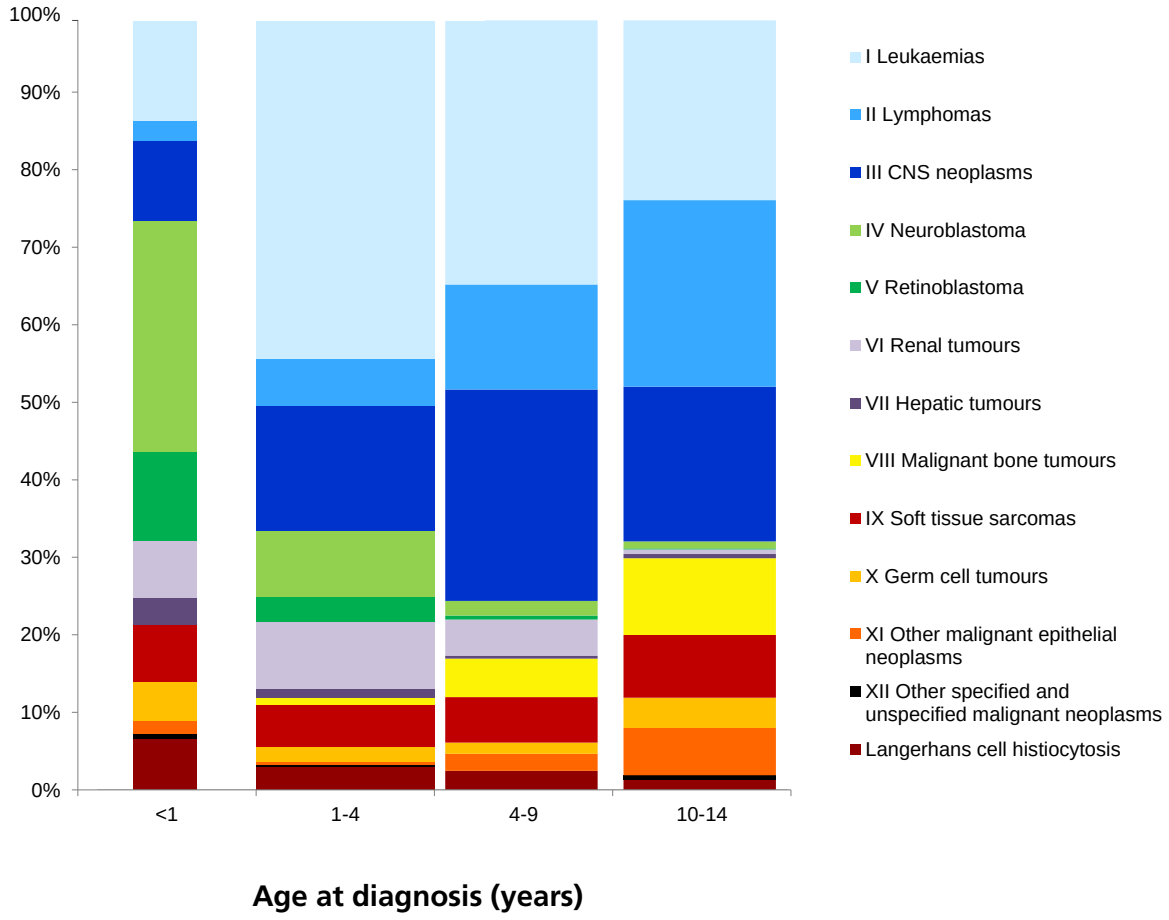
Swiss residents; age at diagnosis 0-14 years; period of diagnosis 1976-2011; all diagnoses (ICCC-3 or Langerhans cell histiocytosis); N=5913

Diagnosis		Total		Age at diagnosis (years)							
		number		<1yr		1-4yrs		5-9yrs		10-14yrs	
		n	%	n	%	n	%	n	%	n	%
I	Leukaemias, myeloproliferative diseases and myelodysplastic diseases	1925	32.6	76	13.0	921	44.4	541	34.1	387	23.2
II	Lymphomas and reticuloendothelial neoplasms	754	12.8	15	2.6	123	5.9	215	13.5	401	24.1
III	Central nervous system neoplasms	1162	19.7	61	10.4	336	16.2	433	27.3	332	19.9
IV	Neuroblastoma and other peripheral nervous cell tumours	397	6.7	176	30.1	176	8.5	30	1.9	15	0.9
V	Retinoblastoma	145	2.5	67	11.5	68	3.3	8	0.5	2	0.1
VI	Renal tumours	307	5.2	44	7.5	179	8.6	74	4.7	10	0.6
VII	Hepatic tumours	58	1.0	20	3.4	23	1.1	6	0.4	9	0.5
VIII	Malignant bone tumours	263	4.4	0	0.0	19	0.9	79	5.0	165	9.9
IX	Soft tissue and other extraosseous sarcomas	385	6.5	44	7.5	113	5.5	93	5.9	135	8.1
X	Germ cell tumours, trophoblastic tumours and neoplasms of gonads	157	2.7	29	5.0	40	1.9	23	1.4	65	3.9
XI	Other malignant epithelial neoplasms and malignant melanomas	155	2.6	10	1.7	8	0.4	35	2.2	102	6.1
XII	Other specified and unspecified malignant neoplasms	17	0.3	4	0.7	4	0.2	0	0.0	9	0.5
	Langerhans cell histiocytosis	188	3.2	39	6.7	63	3.0	51	3.2	35	2.1
	Total	**5913**	**100.0**	**585**	**100.0**	**2073**	**100.0**	**1588**	**100.0**	**1667**	**100.0**

Figure 2 – Main diagnostic groups according to ICCC3, by age at diagnosis (years)

Swiss residents; age at diagnosis 0-14 years; period of diagnosis 1976-2011; all diagnoses (ICCC-3 or Langerhans cell histiocytosis); N=5913

The widths of the columns are proportional to the number of patients.



Follow-up information

The SCCR collects follow-up information for patients in several ways:

1. Clinical follow-up (**Table 4**) is any contact the patient has with the paediatric oncology and haematology centre. Annual clinical follow-up care in paediatric centres usually ends 5-10 years after diagnosis, when the patient is officially discharged or referred to an adult oncology centre, or if the patient dies. Thirty–seven per cent of patients had a clinical follow-up in the past 5 years and another 16% had their last clinical follow-up 6-10 years ago.

2. Long-term epidemiological follow-up for vital status, subsequent neoplasms and current health employs four complementary approaches:

- **Vital status** and current address are updated by contacting municipal population registers. Vital status is known for most cases: among the 5864 patients, 1503 (25.6%) have died, and 252 (4.2%) were lost to follow-up, mostly because they moved abroad. For the other 4109 survivors, vital status has been updated within the last 5 years.
- **Causes of death** are retrieved from Swiss mortality statistics by data linkage.
- **Second primary neoplasms** are detected by regular comparison with cantonal (regional) cancer registries in Switzerland.
- **Morbidity and quality of life** are assessed by postal questionnaires to survivors in the Swiss Childhood Cancer Survivor Study and Childhood Cancer Follow-up Study (SCCSS & CCFU, **Chapter 4**).

Table 4 – Clinical Follow-up information available in the SCCR

Swiss residents; age at diagnosis 0-14 years; period of diagnosis 1976-2011; all diagnoses (ICCC-3 or Langerhans cell histiocytosis); N=5864

Clinical follow-up at paediatric centre	n	%
Last clinical follow-up 2007-2012	2167	37.0
Last clinical follow-up 2002-2006	948	16.2
Last clinical follow-up before 2002	1246	21.2
Died	1503	25.6
TOTAL	**5864***	**100.0**

*We counted patients instead of cases (patients with more than one primary neoplasm are only counted once).

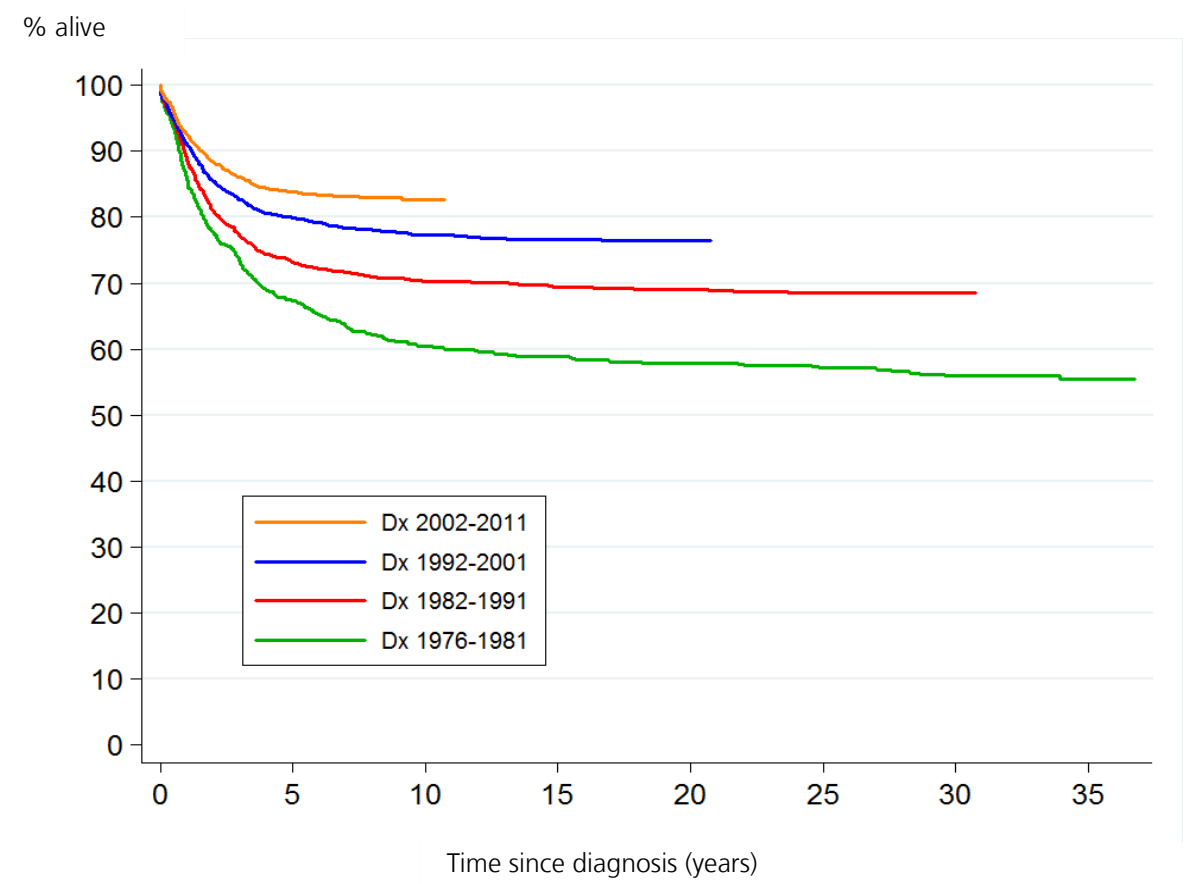
Survival

The following figures present data on the survival of patients registered in the SCCR.

Figure 3 shows an actuarial curve presenting overall survival up to 35 years after diagnosis for patients diagnosed between 1976 and 2011, grouped in four periods. In total, 1503 (25%) children have died. Ten-year survival increased from 60.5% in children diagnosed between 1976 and 1981, 70.3% in children diagnosed between 1982-1991, to 77.3% in children diagnosed between 1992 and 2001, and reached 82.7% in children diagnosed within the last decade.

Figure 3 – Survival of patients in the SCCR, by period of diagnosis

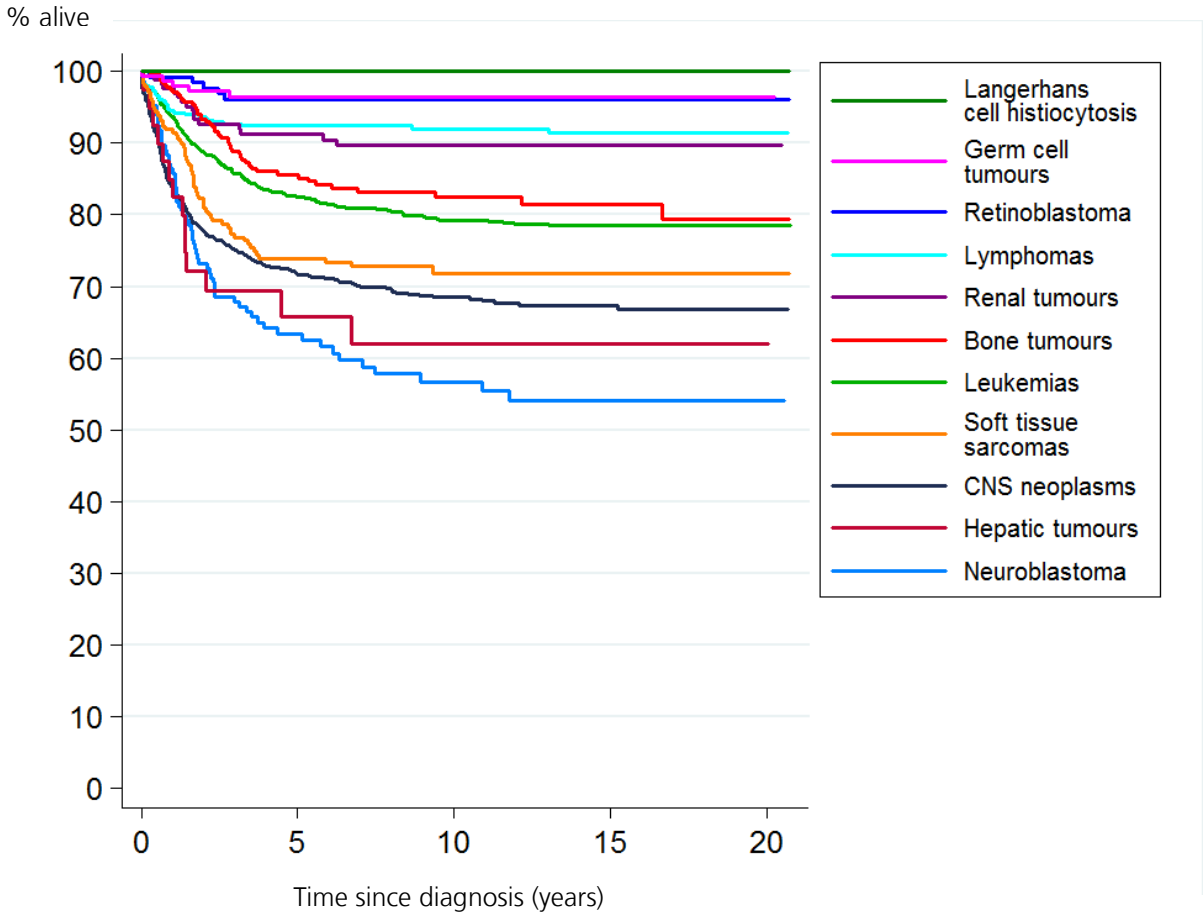
Swiss residents; age at diagnosis 0-14 years; period of diagnosis 1976-2011; all diagnoses (ICCC-3 or Langerhans cell histiocytosis); N=5913; adjusted for sex, age at diagnosis and ICCC-3 groups



Survival varied widely between diagnostic groups. **Figure 4** presents survival by diagnostic group according to ICCC-3 in cases diagnosed between 1992 and 2011. Of these, 756 (19.8%) have died. The following numbers describe five-year survival for each main diagnostic group: 82.6% for cases with leukaemias; 92.4% for those with lymphomas; 71.7% for central nervous system neoplasms; 63.4% for neuroblastoma; 96.1% for retinoblastoma; 91.3% for renal tumours; 65.7% for hepatic tumours; 85.6% for malignant bone tumours; 74.0% for soft tissue sarcomas; 96.4% for germ cell tumours; and 100.0% in Langerhans cell histiocytosis.

Figure 4 – Survival of patients by diagnostic groups according to ICCC-3

Swiss residents; age at diagnosis 0-14 years; period of diagnosis 1992-2011; all diagnoses (ICCC-3 or Langerhans cell histiocytosis); N=3822; adjusted for sex and age at diagnosis



Cancer incidence (2002-2011) in Switzerland, for children aged 0-14 years at diagnosis

Table 5 reports tumours according to ICCC-3 for the last ten years (2002-2011). It describes relative frequency, sex ratio, mean age and incidence. Overall more tumours were diagnosed in boys than girls. This was true for most types of tumours, except neuroblastoma, retinoblastoma, germ cell tumours, and other malignant epithelial neoplasms including malignant melanomas.

The age-standardised incidence (according to the European standard population) of any childhood cancer (not including Langerhans cell histiocytosis) was 16.2 per 100,000 person-years. Incidence was highest among children aged less than 1 year with 24.6 cases per 100,000 person-years (boys 24.2, girls 25.0). Incidence was lowest in 5-9 year olds with 12.8 cases per 100,000 person-years (**Figure 5** shows crude incidence rates and **Figure 6** shows age- and sex-specific incidence rates for age-groups under 15 years).

Table 5 – Number of registered cases in the SCCR for the last 10 years, relative frequency, sex ratio, mean age at diagnosis and incidence standardised according to the European standard population, by diagnostic groups according to ICCC-3

Swiss residents; age at diagnosis 0-14 years; period of diagnosis 2002-2011; all diagnoses (ICCC-3 or Langerhans cell histiocytosis); N=1941

	Diagnosis	n	Relative frequency	Sex ratio (male: female)	Mean age at Dx	Incidence*
I	**Leukaemias, myeloproliferative diseases and myelodysplastic diseases**	**588**	**31.2**	**1.3**	**5.0**	**4.9**
	a. Lymphoid leukaemias	475	80.8	1.3	4.8	4.0
	b. Acute myeloid leukaemias	75	12.8	1.8	7.1	0.6
	c. Chronic myeloproliferative diseases	4	0.7	3.0	11.8	0.03
	d. Myelodysplastic syndrome and other myeloproliferative diseases	24	4.1	1.2	7.1	0.2
	e. Unspecified and other specified leukaemias	10	1.7	0.7	3.1	0.1
II	**Lymphomas and reticuloendothelial neoplasms**	**238**	**12.6**	**1.7**	**10.8**	**2.0**
	a. Hodgkin lymphomas	102	42.9	0.9	12.6	0.9
	b. Non-Hodgkin lymphomas (except Burkitt lymphoma)	76	31.9	3.0	9.0	0.6
	c. Burkitt lymphoma	52	21.8	5.5	7.4	0.4
	d. Miscellaneous lymphoreticular neoplasms	7	2.9	0.8	1.3	0.1
	e. Unspecified lymphomas	1	0.4	0.0	13.6	0.01
III	**CNS and miscellaneous intracranial and intraspinal neoplasms**	**429**	**22.7**	**1.1**	**7.0**	**3.6**
	a. Ependymomas and choroid plexus tumour	34	7.9	1.4	2.4	0.3
	b. Astrocytomas	162	37.8	1.3	7.1	1.4
	c. Intracranial and intraspinal embryonal tumours	102	23.8	1.3	6.1	0.9
	d. Other gliomas	50	11.7	0.6	6.1	0.4
	e. Other specified intracranial and intraspinal neoplasms	71	16.6	0.9	11.2	0.6
	f. Unspecified intracranial and intraspinal neoplasms	10	2.3	1.0	9.8	0.1
IV	**Neuroblastoma and other peripheral nervous cell tumours**	**125**	**6.6**	**0.9**	**1.1**	**1.0**
	a. Neuroblastoma and ganglioneuroblastoma	125	100.0	0.9	1.1	1.0
V	**Retinoblastoma**	**35**	**1.9**	0.7	**1.0**	**0.3**
VI	**Renal tumours**	**95**	**5.0**	1.2	**3.4**	**0.8**
	a. Nephroblastoma and other nonepithelial renal tumours	92	96.8	1.2	3.3	0.8
	b. Renal carcinomas	3	3.2	0.5	12.8	0.03

Table 5 – continued

	Diagnosis	n	Relative frequency	Sex ratio (male: female)	Mean age at Dx	Incidence*
VII	**Hepatic tumours**	**16**	**0.8**	**3.0**	**1.6**	**0.1**
	a. Hepatoblastoma	14	87.5	2.5	1.6	0.1
	b. Hepatic carcinomas	2	12.5	2.0	7.0	0.0
VIII	**Malignant bone tumours**	**90**	**4.8**	**1.0**	**10.6**	**0.75**
	a. Osteosarcomas	40	44.4	0.7	10.9	0.3
	c. Ewing tumour and related sarcomas of bone	49	54.4	1.2	10.2	0.4
	e. Unspecified malignant bone tumours	1	1.1	0.0	14.7	0.0
IX	**Soft tissue and other extraosseous sarcomas**	**138**	**7.3**	**1.3**	**7.6**	**1.2**
	a. Rhabdomyosarcomas	79	57.2	1.3	5.0	0.7
	b. Fibrosarcomas, peripheral nerve sheath tumours and other fibrous neoplasms	8	5.8	1.0	8.1	0.1
	c. Kaposi sarcoma	1	0.7	0.0	10.0	0.0
	d. Other specified soft tissue sarcomas	36	26.1	1.0	11.6	0.30
	e. Unspecified soft tissue sarcomas	14	10.1	2.5	2.6	0.1
X	**Germ cell tumours, trophoblastic tumours, and neoplasms of gonads**	**59**	**3.1**	**0.8**	**8.0**	**0.5**
	a. Intracranial and intraspinal germ cell tumours	13	22.0	1.6	8.7	0.1
	b. Malignant extracranial and extragonadal germ cell tumours	17	28.8	0.4	1.4	0.1
	c. Malignant gonadal germ cell tumours	28	47.5	0.9	10.6	0.2
	d. Gonadal carcinomas	1	1.7	0.0	13.9	0.0
XI	**Other malignant epithelial neoplasms and malignant melanomas**	**68**	**3.6**	**0.9**	**11.3**	**0.6**
	a. Adrenocortical carcinomas	2	2.9	1.0	6.4	0.0
	b. Thyroid carcinomas	14	20.6	0.4	13.1	0.1
	c. Nasopharyngeal carcinomas	1	1.5	0.0	12.2	0.0
	d. Malignant melanomas	24	35.3	1.4	10.6	0.2
	e. Skin carcinomas	9	13.2	1.3	6.2	0.1
	f. Other and unspecified carcinomas	18	26.5	0.8	11.5	0.15
XII	**Other and unspecified malignant neoplasms**	**5**	**0.2**	**1.5**	**0.4**	**0.04**
	a. Other specified malignant tumours	2	40.0	1.0	6.4	0.02
	b. Other unspecified malignant tumours	3	60.0	2.0	0.4	0.03
	Total (not including Langerhans cell histiocytosis)	**1'886**	**100**	**1.2**	**6.8**	**15.7**
	Langerhans cell histiocytosis	55	2.8	1.2	5.0	0.5
	Total (including Langerhans cell histiocytosis)	**1'941**	**100**	**1.2**	**6.8**	**16.1**

* Incidence: newly diagnosed tumours in a one year time period per 100,000 persons (person-years)

Figure 5 – Crude incidence rate (per 100,000 person-years) in Switzerland, by sex and year of diagnosis for the last 20 years

Swiss residents; age at diagnosis 0-14 years; period of diagnosis 1992-2011; all diagnoses (ICCC-3 but not including Langerhans cell histiocytosis); N=3696

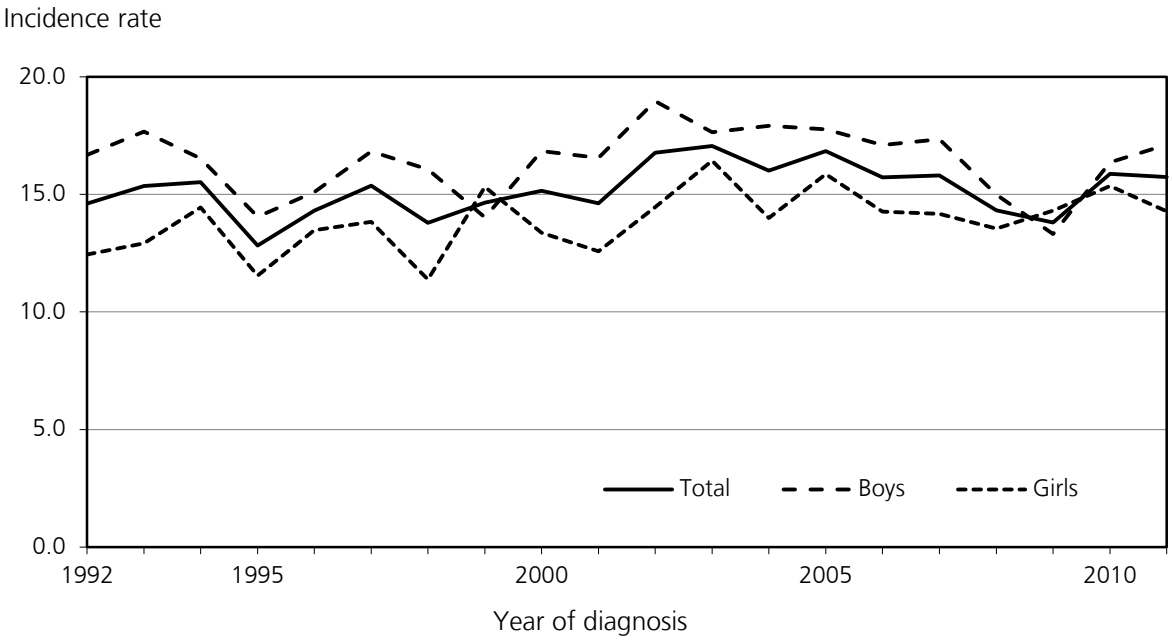
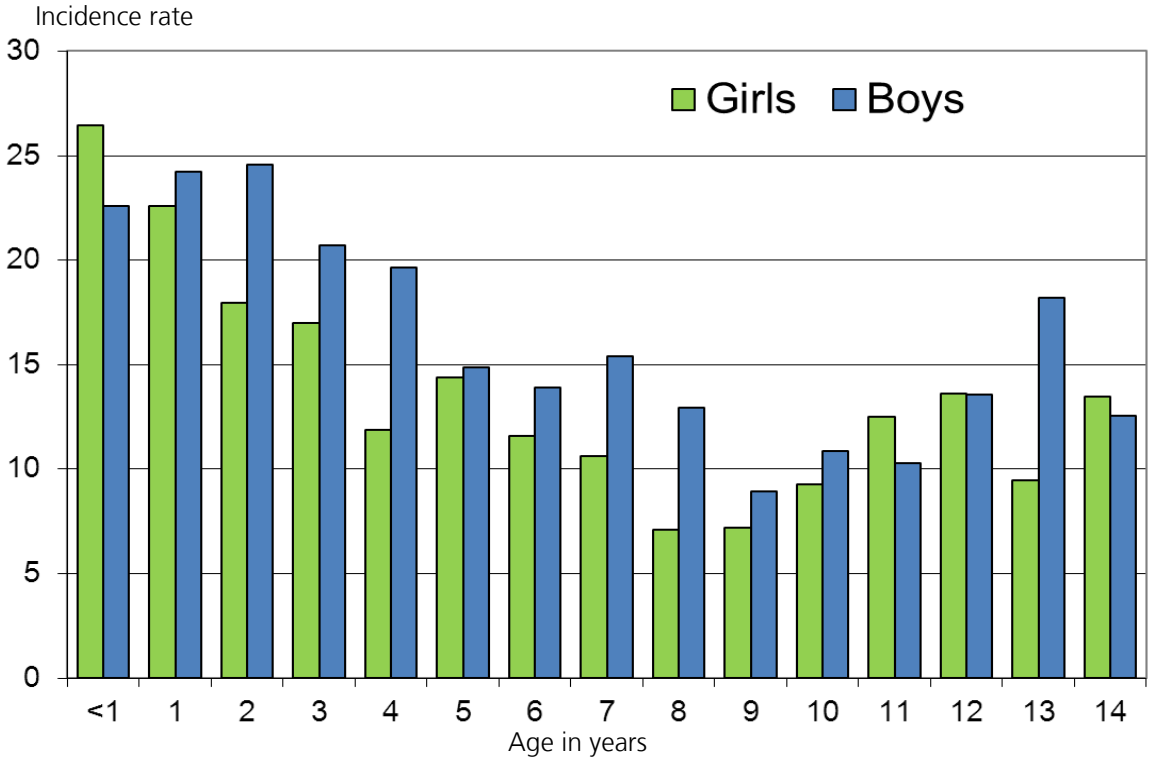


Figure 6 – Age- and sex-specific incidence rates (per 100,000 person-years) in Switzerland for the last 10 years

Swiss residents; age at diagnosis 0-14 years; period of diagnosis 2002-2011; all diagnoses (ICCC-3 but not including Langerhans cell histiocytosis); N=1886



3.3 Swiss residents aged 15-20 years at diagnosis (N=1815)

Table 6 reports cases according to ICCC-3 registered in the last ten years (2002-2011), diagnosed in adolescent patients (aged 15-20 years at diagnosis). It describes relative frequency, sex ratio and mean age at diagnosis. Because data on adolescents is currently not population-based within the SCCR, we do not present incidence rates. In adolescents the sex ratio is closer to 1 than in those aged 0-14 years.

Table 6 – Number of tumours registered in adolescent patients in the SCCR for the last 10 years, relative frequency, sex ratio and mean age at diagnosis, by diagnostic groups according to ICCC-3

Swiss residents; age at diagnosis 15-20 years; period of diagnosis 2002-2011; all diagnoses (ICCC-3 or Langerhans cell histiocytosis); N=569

	Diagnosis	n	Relative frequency	Sex ratio (male: female)	Mean age at Dx
I	**Leukaemias, myeloproliferative diseases and myelodysplastic diseases**	**69***	**12.1**	**1.5**	**16.5**
	a. Lymphoid leukaemias	38	55.1	1.9	16.1
	b. Acute myeloid leukaemias	16	23.2	1.3	15.9
	c. Chronic myeloproliferative diseases	6	8.7	1.0	18.8
	d. Myelodysplastic syndrome and other myeloproliferative diseases	3	4.3	0.5	17.7
	e. Unspecified and other specified leukaemias	1	1.4	0.0	18.9
II	**Lymphomas and reticuloendothelial neoplasms**	**147***	**25.9**	**0.7**	**17.0**
	a. Hodgkin lymphomas	91	61.9	0.6	17.0
	b. Non-Hodgkin lymphomas (except Burkitt lymphoma)	34	23.1	0.9	17.0
	c. Burkitt lymphoma	7	4.8	1.3	18.4
	d. Miscellaneous lymphoreticular neoplasms	1	0.7	0.0	16.6
III	**CNS and miscellaneous intracranial and intraspinal neoplasms**	**94***	**16.5**	**1.0**	**16.7**
	a. Ependymomas and choroid plexus tumour	10	10.6	0.4	18.5
	b. Astrocytomas	32	34.0	0.8	16.7
	c. Intracranial and intraspinal embryonal tumours	17	18.1	1.4	16.0
	d. Other gliomas	7	7.4	1.3	17.1
	e. Other specified intracranial and intraspinal neoplasms	25	26.6	1.3	16.5
	f. Unspecified intracranial and intraspinal neoplasms	2	2.1	1.0	18.5
IV	**Neuroblastoma and other peripheral nervous cell tumours**	**0**	**0.0**	**0.0**	**0.0**
V	**Retinoblastoma**	**0**	**0.0**	**0.0**	**0.0**
VI	**Renal tumours**	**9**	**1.6**	**0.8**	**17.1**
	a. Nephroblastoma and other nonepithelial renal tumours	4	44.4	1.0	16.4
	b. Renal carcinomas	5	55.6	0.7	17.5

Table 6 – continued

	Diagnosis	n	Relative frequency	Sex ratio (male: female)	Mean age at Dx
VII	**Hepatic tumours**	**5**	**0.9**	**1.5**	**16.1**
	a. Hepatoblastoma	5	100.0	1.5	16.1
VIII	**Malignant bone tumours**	**47***	**8.3**	**1.8**	**16.3**
	a. Osteosarcomas	34	72.3	1.8	16.3
	c. Ewing tumour and related sarcomas of bone	10	29.4	1.5	16.6
	d. Other specified malignant bone tumours	2	20.0	1.0	16.7
IX	**Soft tissue and other extraosseous sarcomas**	**37***	**6.5**	**0.7**	**16.8**
	a. Rhabdomyosarcomas	16	43.2	0.8	16.0
	d. Other specified soft tissue sarcomas	17	45.9	0.5	18.0
	e. Unspecified soft tissue sarcomas	3	8.1	0.5	16.8
X	**Germ cell tumours, trophoblastic tumours, and neoplasms of gonads**	**46***	**8.1**	**10.5**	**19.1**
	a. Intracranial and intraspinal germ cell tumours	2	4.3	0.0	18.0
	c. Malignant gonadal germ cell tumours	40	87.0	12.3	19.1
	d. Gonadal carcinomas	1	2.2	0.0	15.4
XI	**Other malignant epithelial neoplasms and malignant melanomas**	**112***	**19.7**	**0.8**	**18.6**
	a. Adrenocortical carcinomas	1	0.9	0.0	17.0
	b. Thyroid carcinomas	21	18.8	0.3	18.4
	c. Nasopharyngeal carcinomas	3	2.7	0.0	17.9
	d. Malignant melanomas	51	45.5	0.7	18.7
	e. Skin carcinoma	8	7.1	0.3	18.6
	f. Other and unspecified carcinomas	18	16.1	3.5	18.2
XII	**Other and unspecified malignant neoplasms**	**2**	**0.4**	**1.0**	**18.0**
	a. Other specified malignant tumours	2	100.0	1.0	18.0
	Total (not including Langerhans cell histiocytosis)	**568**	**100.0**	**1.1**	**17.6**
	Langerhans cell histiocytosis	1	0.2	0.0	17.0
	Total (including Langerhans cell histiocytosis)	**569**	**100.0**	**1.1**	**17.6**

*This total includes tumours where only main group is available due to lack of detailed medical information

4. Research projects on childhood cancer

Table 7 summarises recent or current research projects of the childhood cancer registry. All projects are described in more detail in the remainder of **Chapter 4**, and additional information is available from the references and from the investigators. We thank the supporters listed in **Table 7** for their generous contributions towards the research projects.

Table 7 – Research projects at the SCCR

No	Project name	Funding	Primary investigator	Study Type	Study period
1	Swiss Childhood Cancer Survivor Study (SCCSS)	Swiss Cancer League Cancer League Aargau Cancer League Zürich Swiss Bridge Foundation	Von der Weid NX Kuehni CE	Cohort study	01.2006-12.2013
2	An international case-control study on brain tumours in children and adolescents (CEFALO)	Swiss National Science Foundation Mobilfunkstiftung	Röösli M	Case-control study	10.2005-12.2008
3	Childhood cancer and nuclear power plants in Switzerland (CANUPIS)	Federal Office of Public Health Swiss Cancer League	Kuehni CE	Cohort study	09.2008-12.2010
4	Follow-up care after childhood and young adult cancer (CCFU)	Swiss National Science Foundation	Michel G	Cohort study	08.2009-07.2014
5	Risk of cancer and long-term mortality in children treated with Growth Hormone: Swiss participation in the EU FP7 project "SAGhE"	EU FP7 Swiss Cancer League	Mullis PE Kuehni CE	Cohort study	01.2010-12.2013
6	PanCare childhood and adolescent cancer survivor care and follow-up studies (PanCareSurFup)	EU FP7 Cancer Research Switzerland	Kuehni CE Michel G	Cohort study	02.2011-01.2016
7	Childhood cancer and vicinity of residence to petrol stations and major roads: a census-based nationwide cohort study (PETROL)	Federal Office of Public Health	Kuehni CE Feller M	Cohort study	06.2010-12.2012
8	Developing a radon exposure model to predict domestic radon exposure for Swiss children	Swiss National Science Foundation	Röösli M	Cohort study	01.2011-12.2013
9	Effectiveness of transition from paediatric to adult care after childhood cancer	Swiss Cancer League	Michel G	Cohort study	04.2011-03.2014
10	Mortality and second primary neoplasms after cancer in childhood and adolescence	Swiss National Science Foundation Swiss Bridge Foundation	Kuehni CE Michel G Egger M	Cohort study	11.2012-10.2015
11	Childhood cancer and geographically defined exposures in Switzerland: a census-based nationwide cohort study	Federal Office of Public Health	Kuehni CE Spycher B	Cohort study	01.2013-11.2014
12	The role of population mixing and exposure to infections in the aetiology of childhood leukaemia: a national cohort study	Cancer Research Switzerland	Spycher B	Cohort study	01.2013-12.2014

4.1 Swiss Childhood Cancer Survivor Study (SCCSS)

Background: Thanks to therapeutic improvements in the past decades, survival rates for childhood cancer now exceed 80%, leading to a growing population of long-term survivors. However, cancer and cancer treatments have been associated with adverse late effects and the health and quality of life of survivors are of increasing concern. In Switzerland and other countries, comprehensive data on the burden of late effects of childhood cancer and its risk factors, as well as data on the use of follow-up care in long-term survivors is scarce.

Objectives: This project investigates long-term outcomes of childhood cancer survivors, diagnosed with cancer before the age of 21 years and who survived for more than 5 years. It studies the incidence and spectrum of various somatic and psycho-social outcomes including late mortality, second primary malignancies, somatic health and medication, mental health, educational achievements, health related quality of life, and their association with a number of risk factors assessed prospectively at time of diagnosis (tumour, treatment modalities, demographic characteristics). Current practices of health-care provision and health behaviour in long-term survivors are also investigated.

Methods: This is a prospective cohort study based on the population of children and adolescents registered in the SCCR. All individuals who have been diagnosed with cancer before 31 December 2005 when aged <21 years, who are still alive, and who were Swiss residents at time of diagnosis are eligible for the study. A detailed questionnaire is being sent to all participants. Questionnaire data are validated with information provided by general practitioners and hospital records. For comparison, the same questionnaire is sent to all siblings of childhood cancer survivors who answered the questionnaire.

Current status of the project: By 31 December 2012, we have contacted 2930 survivors aged 0-16 years at time of diagnosis. Of these, 2160 answered our questionnaire (74%). These include 1284 adult survivors aged >20 years (76% of those contacted), as well as 447 adolescent survivors aged 15-20 years (67% of those contacted) and 429 parents of children agend <15 years (73% of those contacted). In autumn 2012, we started to contact former patients who were diagnosed at age 16-20 years. Of the 1530 siblings that could be traced and contacted, a total of 819 (54%) answered the questionnaire. Among them were 578 adults (59%), 135 adolescents (44%) and 106 parents of children (42%).

Applicants: Kuehni CE, Egger M, Zwahlen M, Rebholz CE, Rueegg CS. Institute of Social and Preventive Medicine, University of Bern; von der Weid NX. Paediatric Oncology, University Children's Hospital Basel (UKBB); Niggli F, Bergstraesser E. University Children's Hospital, Zurich; Angst R. Children's Hospital Aarau; Probst-Hensch N. Swiss Tropical & Public Health Institute, University of Basel.

Project team: Kuehni CE, Wengenroth L, Rueegg CS, Essig S, Koch J, Liechti F, Brantschen E, Michel G. Institute of Social and Preventive Medicine, University of Bern; von der Weid NX. Paediatric Oncology, University Children's Hospital Basel (UKBB)

Funding: Swiss Cancer League (Grant No KLS 01605-10-2004 and KLS 2215-02-2008), Stiftung zur Krebsbekämpfung, Swiss Bridge Foundation, Bernese Cancer League, Cancer League Zurich and Cancer League Aargau.

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Laura Wengenroth (lwengenroth@ispm.unibe.ch)

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Gianinazzi ME, Rueegg CS, Wengenroth L, Bergstraesser E, Rischewski J, Ammann RA, Kuehni CE, Michel G. Adolescent survivors of childhood cancer: are they vulnerable for psychological distress? *Psycho-Oncology 2013; doi:10.1002/pon.3249.*

Publications (submitted):

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Gianinazzi ME, Rueegg CS, Wengenroth L, Niggli FK, Kuehni CE, Michel G. Psychological care in adult survivors of childhood cancer and siblings: the Swiss Childhood Cancer Survivor Study.

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4.2 An international case-control study on brain tumours in children and adolescents (CEFALO)

Background: It was hypothesized that children might be more vulnerable to radio frequency electromagnetic field exposures from mobile telephones than adults. Decision-makers issued conflicting recommendations because not enough data was available, which led to anxiety and insecurity in the population. In their 2006 research agenda, WHO put a high priority on a case-control study on radio frequency electromagnetic fields and childhood brain tumours in order to address these concerns.

Objectives: The study was designed to determine if use of mobile telephones increases risk of brain tumours in children or adolescents. In addition, other potential risk factors for childhood brain tumours were investigated.

Study design: The questions were investigated through an international case-control study in Denmark, Norway, Sweden and Switzerland. Cases were identified by combining registry data and information from the wards where the cases were treated (e.g. Swiss Paediatric Oncology Group). All incident cases of brain tumour at age 7-19 years between May 2004

and April 2008 were invited to participate. In total, the study included 550 cases of brain tumours in all participating countries; 100 originated in Switzerland. For each case, two control persons were randomly selected from the general population, matched on age, sex and geographic region.

Exposure assessment: Information on the extent of exposure to radio frequency fields from mobile phones, and on other known and suspected risk factors for childhood brain tumours was obtained by means of computer assisted personal interviews. Objective information on the frequency and duration of mobile phone use was obtained from mobile phone operators and from the information stored in the telephone in current use.

Data analyses: The data was analysed using statistical methods for case-control studies, primarily via conditional logistic regression models adjusted for potential confounders.

Current status of the project: Data collection has been completed for cases and controls and several papers have been published. Additional analyses are still on-going.

Applicants: Röösli M. Swiss Tropical and Public Health Institute Basel; Kuehni CE. Institute of Social and Preventive Medicine, University of Bern; Grotzer M. University Children's Hospital, Zurich; Feychting M. Karolinska Institutet, Stockholm; Tynes T. Cancer Registry of Norway, Oslo; von der Weid NX. Paediatric Oncology, University Children's Hospital Basel (UKBB); Schuetz J. International Agency for Research on Cancer (IARC), Section of Environment and Radiation, Lyon, France.

Project team: Aydin D, Röösli M. Swiss Tropical and Public Health Institute Basel; Kuehni CE. Institute of Social and Preventive Medicine, University of Bern.

Funding: Swiss Federal Office of Public Health (Grant No 05.001626), Swiss Research Foundation on Mobile Communication (Grant No A2006.18), and Swiss National Science Foundation (Grant No PDFMP3_122873).

Contact: Martin Röösli (martin.roosli@unibas.ch)

Publications (published):

Aydin D, Feychting M, Schüz J, Tynes T, Andresen TV, Schmidt LS, Poulsen AH, Johansen C, Prochazka M, Lannering B, Klaeboe L, Eggen T, Jenni D, Grotzer M, von der Weid NX, Kuehni CE, Röösli M. Mobile phone use and brain tumors in children and adolescents: a multicenter case-control study. *Journal of the National Cancer Institute 2011; 103:* 1264-1276.

Aydin D, Feychting M, Schüz J, Andersen TV, Poulsen AH, Prochazka M, Klæboe L, Kuehni CE, Tynes T, Röösli M. Impact of random and systematic recall errors and of selection bias in case-control studies on mobile phone use and brain tumours in adolescents (CEFALO study). *Bioelectromagnetics 2011; 32*: 396-407.

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Aydin D, Feychting M, Schüz J, Röösli M. Childhood brain tumours and use of mobile phones: Comparison of a case-control study with incidence data. *Environmental Health 2012; 11*: 35.

Christensen JS, Mortensen LH, Röösli M, Feychting M, Tynes T, Andersen TV, Schmidt LS, Poulsen AH, Aydin D, Kuehni CE, Prochazka M, Lannering B, Klaeboe L, Eggen T, Schüz J. Brain tumors in children and adolescents and exposure to animals and farm life: a multicenter case-control study (CEFALO). *Cancer Causes and Control 2012; 23*: 1463-1473.

Publications (submitted):

Andersen TV, Schmidt LS, Poulsen AH, Feychting M, Röösli M, Tynes T, Aydin D, Prochazka M, Lannering B, Klæboe L, Eggen T, Kuehni CE, Schmiegelow K, Schüz J. Patterns of exposure to infectious diseases and social contact in early life and risk of brain tumours in children and adolescents: an International Case-Control Study (CEFALO).

4.3 Childhood cancer and nuclear power plants in Switzerland (CANUPIS)

Background: Since a cluster of leukaemia cases around Sellafield was reported in 1984, many studies have investigated associations between childhood cancer and residence near nuclear power plants (NPPs). The results of these studies were heterogeneous and many found weak positive associations.

Objectives: To investigate possible associations between residence near a NPP and the risk of childhood cancer, and childhood leukaemia in particular.

Methods: This was a census-based cohort study with national coverage. To estimate person-years at risk, the study used the Swiss National Cohort (SNC), a long-term, census-based, multipurpose cohort and research platform that includes all Swiss inhabitants. Cases were identified from the Swiss Childhood Cancer Registry (SCCR) and all cases born between January 1985 and December 2007 and aged 0-15 years at diagnosis were included. For these individuals we reconstructed address histories back to birth by contacting municipal population registers. We geocoded all addresses and calculated distances to nearest NPPs. Using Poisson regression we calculated incidence rate ratios (IRRs) comparing the risk of cancer in children living 0-5 km, 5-10 km, 10-15 km to those living >15 km from a NPP at birth (primary analysis) and at diagnosis (secondary analysis). The following potential confounders were included: background ionizing radiation (cosmic, terrestrial artificial and total radiation); electromagnetic radiation from radio and TV transmitters, railway tracks, and high voltage power lines; distance to major roads; agricultural pesticides (based on land-use statistics); and, community level socio-economic and demographic indicators (degree of urbanisation, Sotomo-Index and average number of children per household). We assessed robustness of results in numerous sensitivity analyses.

Current status of project: We included 2925 children diagnosed with cancer over 21 million person-years of follow-up; 953 (32.6%) were diagnosed with leukaemia. Eight and 12 children who were diagnosed with leukaemia at ages 0–4 and 0–15 years, and 18 and 31 children who were diagnosed with any type of cancer lived within 5km of a NPP. Compared with children born >15km away, the IRRs (95% CI) for leukaemia in 0–4 and 0–15 year olds were 1.20 (0.60–2.41) and 1.05 (0.60–1.86), respectively. For any cancer, corresponding IRRs were 0.97 (0.61–1.54) and 0.89 (0.63–1.27). There was no evidence of a dose–response relationship with distance (P>0.30). Results were similar for residence at

diagnosis and at birth, and when adjusted for potential confounders. Results from sensitivity analyses were consistent with main results.

Conclusions and significance: This study found little evidence for an association between risk of childhood cancer and residence near NPPs. This study contributes importantly to the current evidence base in this field of research. Because the study was nationwide, and thus virtually free of selection bias, used exact geocodes of place of residence at birth and at diagnosis, and adjusted for a wide range of confounders, it overcame some significant methodological limitations of previous studies.

Applicants: Kuehni CE. Institute of Social and Preventive Medicine, University of Bern; Röösli M. Swiss Tropical and Public Health Institute, University of Basel; von der Weid NX. Paediatric Oncology, University Children's Hospital Basel (UKBB); Hengartner H. Children's Hospital, St. Gallen; Niggli F. University Children's Hospital, Zurich; Egger M. Institute of Social and Preventive Medicine, University of Bern.

Project team: Feller M, Kuehni CE, Spycher BD, Zwahlen M, Gueler A, Institute of Social and Preventive Medicine, University of Bern; Röösli M. Swiss Tropical and Public Health Institute, University of Basel.

Funding: Federal Office of Public Health (Grant No 08.001616) and Swiss Cancer League (Grant No KLS 02224-03-2008).

Contact: Claudia Kuehni (kuehni@ispm.unibe.ch)

Publications:

Spycher BD*, Feller M*, Zwahlen M, Röösli M, von der Weid N, Hengartner H, Egger M, Kuehni CE. Childhood cancer and nuclear power plants in Switzerland: a census-based cohort study. *International Journal of Epidemiology 2011; 40:* 1247-1260. *shared first authorship with equal contributions

Spycher BD, Kuehni CE, Zwahlen M, Egger M. Authors' response to: Childhood cancer and nuclear power plants in Switzerland: a census-based cohort study. *International Journal of Epidemiology 2012; 41:* 321-322.

Kuehni CE, Feller M, Egger M. Response to: Sufficient statistical power for CANUPIS? *Schweizer Krebsbulletin 2009;* 4.09: 301.

4.4 Follow-up care after childhood and young adult cancer (CCFU)

Background: Treatment for cancer in children and young adults has greatly improved and most patients are being cured today. However, more than 50% of survivors of childhood cancer suffer from late effects. To detect and treat late effects as early as possible, survivors must continue to have follow-up care long after their cancer has been cured. Various models of follow-up care have been described, but so far none has been implemented in Switzerland. While follow-up care needs to be constantly updated to meet the current status of research, survivor participation is only ensured if follow-up is convenient.

Objectives: 1) To compare the advantages and disadvantages of follow-up care models currently used in Europe; 2) To determine the current availability and use of follow-up care in survivors of childhood and young adult cancers in Switzerland; and, 3) To determine the advantages and disadvantages of follow-up care models as perceived by survivors, oncologists and family practitioners, and to compare their views and opinions.

Methods: For part 1), we invited 198 clinics and follow-up programmes in Europe to complete a questionnaire survey describing the follow-up care available at their institution. For part 2), we analysed the current use of follow-up care together with the psychological well-being in childhood cancer survivors, using data from the Swiss Childhood Cancer Survivor Study (SCCSS). In part 3), a questionnaire survey assessed opinions and perspectives on both, currently used and desired optimal follow-up care. The sample includes childhood, adolescent and young adult cancer survivors diagnosed with cancer between 1990 and 2005 and aged <25 years, who survived for >5 years and who are currently aged 11+ years. In addition, paediatric and adult oncologists/haematologists and family practitioners have completed a questionnaire.

Rationale and significance: This project provides an overview of follow-up care in Europe and will describe survivor, oncologist and family practitioner preferences for follow-up care models in Switzerland. We will determine the differences between the three groups in order to improve follow-up care and adapt it to differing preferences. The project will provide the basis for the development of a standardised model of follow-up care for childhood cancer survivors in Switzerland.

Current status of project: A first paper on follow-up care after childhood cancer in Europe has been published. The questionnaire survey on follow-up care after childhood cancer has been completed for survivors of childhood cancer, paediatric and medical oncologists, and general practitioners, but is still on-going for parents of childhood cancer survivors and survivors of adolescent and young adult cancer. Papers on the use of follow-up care by survivors have been published.

Applicant: Michel G. Institute of Social and Preventive Medicine, University of Bern.

Project team: Michel G, Kuehni CE, Lupatsch J, Heg-Bachar Z. Institute of Social and Preventive Medicine, University of Bern; von der Weid NX. Paediatric Oncology, University Children's Hospital Basel (UKBB); Niggli F. University Children's Hospital, Zurich.

Funding: Swiss National Science Foundation (Division Individual Funding "Ambizione" Grant No PZ00P3_121682/1 and PZ00P3_141722/1).

Collaborations: Eiser C, Greenfield D. Child and Family Research Group, University of Sheffield; Hjorth L, Skinner R, Haupt R, PanCare (European network of professionals, survivors and their families established to ensure that every European survivor of childhood and adolescent cancer receives optimal long-term care).

Contact: Gisela Michel (michel@ispm.unibe.ch)

Publications (published):

Michel G, Rebholz CE, von der Weid NX, Bergstraesser E, Kuehni CE. Psychological distress in adult survivors of childhood cancer: the Swiss Childhood Cancer Survivor Study. *Journal of Clinical Oncology 2010; 28:* 1740-1747.

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Michel G, Greenfield D, Absolom K, Eiser C. Follow-up care after childhood and young adult cancer: Satisfaction and associations with coping style. *Psycho-Oncology 2011; 20:* 813-822.

Rebholz CE, von der Weid NX, Michel G. Niggli F, Kuehni CE. Follow-up care amongst long-term childhood cancer survivors: a report from the Swiss Childhood Cancer Survivor Study. *European Journal of Cancer 2011; 47:* 221-229.

Michel G. Nachsorge nach Krebs im Kindesalter – Ein neues Feld für die Pflege? Onkologiepflege 2011. 3, 20-23.

Michel G. Nachsorge nach Krebs im Kindesalter. Schweizer Krebsbulletin 2012. 3, 212-213.

Essig S, von der Weid NX, Skinner R, Kuehni CE, Michel G. Follow-up programs for childhood cancer survivors in Europe: a questionnaire survey. *PLoS ONE 2012; 7*: e53201.

Publications (submitted):

Singer S, Gianinazzi ME, Hohn A, Kuehni CE, Michel G. GP-led follow-up after childhood cancer – a systematic review.

Heg Z, Gianinazzi ME, Rueegg CS, Bergstraesser E, von der Weid NX, Tinner EM, Kuehni CE, Michel G. Longitudinal changes in psychological distress in childhood cancer survivors.

Lupatsch J, Wengenroth L, Rueegg CS, Teuffel MO, Gumy-Pause F, Kuehni CE, Michel G. Follow-up care of adolescent cancer survivors: the role of health-beliefs.

4.5 Risk of cancer and long-term mortality in children treated with growth hormone: Swiss participation in the EU FP7 project "SAGhE"

Background: Recombinant human growth hormone (GH) was initially used to treat cases of primary severe growth hormone deficiency (GHD) but its uses have multiplied. GHD is the most common endocrine late effect of childhood cancer treatment, especially after brain tumours and cranial irradiation. Efficacy of GH treatment in children with severe GHD is undisputed and short term safety during treatment is satisfactory. Data on efficacy for other indications, association with quality of life and long-term safety are scarce. Several experimental studies have raised concerns about cancer risk and long-term mortality. Therefore, an international consortium with investigators from nine countries decided to study "Safety and Appropriateness of Growth hormone treatments in Europe" (SAGhE).

Objectives: To establish a cohort of young adults treated with GH in childhood due to different diagnoses; describe the indications and frequency of GH use for children in Switzerland since 1985; assess long-term efficacy and quality of life in adulthood after GH-treatment in childhood; and to investigate long-term safety of GH-treatment in childhood, in particular risk of cancer and mortality.

Methods: To identify all eligible patients, we collect information from the following sources: a) patients treated in all paediatric endocrinology centres in Switzerland; b) registries (the SCCR and the Swiss Paediatric Renal Registry) and industrial databases. Relevant data are extracted from hospital records. Quality of life is assessed via questionnaire surveys. Incident cancers are assessed via linkage with the SCCR and cantonal cancer registries and via questionnaire survey. Date and place of death is obtained via municipal population registers, causes of death are obtained from the Swiss Federal Statistical Office. The risk of cancer and mortality in the cohort is compared to the risk in the general population by calculating standardized incidence ratios and standardized mortality ratios. For diagnoses with increased baseline risks (childhood cancer survivors, chronic renal failure), we compare risk in GH-treated patients to that of untreated patients with similar diagnoses.

Rationale and significance: The project will describe the use of GH in Switzerland and analyse long-term safety in the context of a high-quality international collaborative study. Results will be presented to the public, guidelines committees and health authorities and will likely influence future recommendations for treatment with GH in children, particularly in children suffering from cancer. Furthermore, prospective data collection will continue and serve as a resource for future research.

Current status of project: We identified 1692 patients treated with GH during childhood. Patients older than 18 years were included in the SAGhE study (N=754). We completed data collection for this age group. We assessed health related quality of life (HRQoL) for patients over 18 years via postal questionnaire. A total of 610 patients were eligible and 333 patients answered the questionnaire (response rate 55%). We linked the growth registry with the SCCR to identify incident cancer during childhood. A linkage with cantonal cancer registries to detect incident cancers in adulthood is still in process. Only 2% of the patients have died (N=14).

Applicants: Mullis PE. Department for Paediatric Endocrinology, Diabetology and Metabolism, University Children's Hospital, Bern; Kuehni CE, Bohlius J. Institute of Social and Preventive Medicine, University of Bern; Grotzer M. University Children's Hospital, Zurich; Clough-Gorr K. NICER, Institute of Social and Preventive Medicine, University of Zurich; Stettler C. Division of Endocrinology, Diabetes, and Clinical Nutrition, University Hospital of Bern.

Project team: Sommer G, Kuonen R, Kuehni CE. Institute of Social and Preventive Medicine, University of Bern; Mullis PE. Department for Paediatric Endocrinology, Diabetology and Metabolism, University Children's Hospital, Inselspital Bern.

Funding: European Union FP7: HEALTH.2007-3.1-5: Better use of medicines, Swiss Cancer League (Grant No KLS 02586-02-2010 and KLS 2948-02-2012).

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Publications: Expected for 2013-2014.

Published abstracts:

Sommer G, Kuehni CE, Karabulut F, Stettler C, Mullis PE, for the Swiss Association for Paediatric Endocrinology and Diabetology. The Swiss Growth Registry: aims, methods and first results. *Swiss Medical Weekly 2012*; 142: 8S.

Karabulut F, Sommer G, Mullis PE, Kuehni CE. Quality of life of young adults treated with recombinant human Growth Hormone during childhood. *Swiss Medical Weekly 2012*; 142: 19S.

4.6 PanCare childhood and adolescent cancer survivor care and follow-up studies (PanCareSurFup)

Background: Long-term survival after childhood cancer exceeds 80%, but two third of survivors develop chronic conditions. Also late mortality is increased as a consequence of the cancer and its treatment. More than ten years after diagnosis, deaths from second primary cancers and circulatory causes predominate. There is thus a compelling need to identify avoidable risk factors for these late effects. Due to small numbers of survivors in single countries, a combination of datasets is essential to tackle these questions.

Objectives: 1) To establish a cohort of 5-year survivors of childhood cancer; 2) to analyse incidence and risk factors for second primary cancers, late cardiovascular diseases and late mortality; 3) to perform nested case-control studies on second primary sarcomas, second primary carcinomas and late cardiovascular diseases; and 4) to develop guidelines for the clinical follow-up of survivors.

Methods: 1) The cohorts of survivors of childhood cancer of the 11 participating European countries will be combined into a pan-European "PanCareSurFup cohort". 2) For all cohort members, we are collecting vital status and date of death via municipal population registers and Swiss mortality statistics. Cardiovascular late effects and second primary cancers are identified via: a) questionnaires to all survivors; b) mortality records (for deceased); and, c) linkage with cantonal cancer registries (for second primary cancers). Patient-reported diseases from the questionnaire are validated with medical records. 3) Case-control studies: From the cohort, Switzerland will sample 50 cases with severe cardiovascular disease, 55 cases with second primary sarcoma or carcinoma and 105 controls. For these we will extract details of radio- and chemotherapy from medical records, and assess current health problems and environmental, social and lifestyle risk factors by interview. 4) In close collaboration with experts from across Europe, we will write systematic reviews to develop evidence-based, standardised guidelines.

Rationale and significance: This research project provides a unique opportunity to study the most severe and life threatening late effects of childhood and adolescent cancer in an international setting that maximises statistical power and generalizability of results. The identification of avoidable causes for cardiovascular late effects and second primary cancers will allow treatment to be adapted for new patients. The goal is maximal cure rates with minimal long-term side effects.

Current status of project: We included 4760 5-year survivors from Switzerland into the "PanCareSurFup" cohort. For all cohort members, we updated vital status, and ascertained date and cause of death. The questionnaire survey will be completed in 2013. By December 2012, we identified 316 patients reporting cardiovascular problems in the questionnaire. Additional 59 survivors were identified via the SCCR and 26 by linking with the Swiss mortality statistics. To validate outcomes, we are contacting general practitioners and performing phone interviews with survivors. We identified 95 survivors who developed a second primary neoplasm. Linkage with cantonal cancer registries to detect additional second primary cancers is in process.

Applicants: Kuehni C, Michel G, Institute of Social and Preventive Medicine (ISPM) University of Bern, von der Weid N, Paediatric Oncology, University Children's Hospital Basel (UKBB), Bergstraesser E, Centre of clinical research, University of Zurich, Kretschmar O, Paediatric cardiology, University of Zurich.

Project team: Kuehni C, Michel G, Hau E, Schindler M. ISPM, University of Bern, von der Weid NX, Paediatric Oncology, University Children's Hospital Basel (UKBB), Bergsträsser E, Centre of clinical research, University of Zurich, Kretschmar O, Pediatric cardiology, University of Zurich

Funding: European Union FP7: HEALTH.2010.2.4.1-7: Predicting long-term side effects to cancer therapy. Cancer Research Switzerland (Grant No KFS 02783-02-2011).

Contact: Eva Hau (ehau@ispm.unibe.ch); Claudia Kuehni (kuehni@ispm.unibe.ch)

Publication (in preparation):

Hau EM, Berner L, Essig S, Michel G, Bergstraesser E, Kuehni CE. Validation of self-reported cardiovascular problems by contacting general practitioners: Feasibility in Switzerland.

4.7 Childhood cancer and vicinity of residence to petrol stations and roads: census-based nationwide cohort study (PETROL)

Background: Benzene is one of the most common traffic-related air-pollutants; it is haematotoxic and an established human carcinogen. Its association with acute myeloid leukaemia is well documented in adults but data on children are scarce. To our knowledge, no cohort studies have investigated potential associations between benzene exposure and childhood cancer in children.

Objective: To examine whether 1) residence in the proximity of petrol stations, motor vehicle service stations or major roads, and 2) parental profession-related exposure to benzene is associated with a higher risk of cancer, particularly leukaemia, in children and adolescents.

Methods: The study includes all children born between January 1985 and December 2008, aged 0-19 years at diagnosis and resident in Switzerland (N=5300). Analyses will be based on information obtained from the SCCR, the Swiss National Birth Registry (NBR) and the Swiss National Cohort (SNC), a long-term, census-based cohort that includes all Swiss inhabitants. All addresses will be geocoded to assess their proximity to petrol stations,

motor vehicle service stations and major roads. We will consider place of residence at birth and at diagnosis separately. Geographic data on petrol and motor vehicle service stations will be obtained from the census of businesses; data on roads from the Tele Atlas database. Data on parental occupation during the 1990 and 2000 censuses will be obtained from the SNC and will allow us to identify children whose parents were exposed to benzene at work. The data will be analysed using Poisson regression models, adjusting for socio-economic status, parental age at birth, birth weight and length, birth order and number of siblings.

Rational and Significance: Traffic-related pollution and its effects on health are a major public health issue because a substantial proportion of the population is exposed. This unique, large-scale study will help clarify whether traffic-related air pollution has an impact on the incidence of childhood cancer in the general population.

Current status of project: Most of the preparatory work has been completed. We have obtained geocoded address of residence at diagnosis (94%) and birth (73%) for most eligible cases. Distances to nearest petrol stations, motor vehicle service stations and major roads have been calculated and associations with cancer risk are being analysed. We are collaborating with the Utrecht University, Holland, to identify occupations with high benzene exposure and analyses of these data will begin shortly.

Applicants: Feller M, Spoerri A. Institute of Social and Preventive Medicine, University of Bern; von der Weid NX. Paediatric Oncology, University Children's Hospital Basel (UKBB); Zwahlen M, Egger M, Kuehni CE. Institute of Social and Preventive Medicine, University of Bern.

Project team: Spycher BD, Spoerri A, Zwahlen M, Gueler A, Kuehni CE. Institute of Social and Preventive Medicine, University of Bern.

Funding: Federal Office of Public Health (Grant No 10.002946).

Contact: Claudia Kuehni (kuehni@ispm.unibe.ch); Ben Spycher (bspycher@ispm.unibe.ch)

Publications: Expected for 2013.

4.8 Developing a model to predict domestic radon exposure for Swiss children

Background: Radon is associated with lung cancers in adults, but less is known about its association with childhood cancers. Most studies published on this issue so far are ecological and do not control for confounders, or they are case-control studies with inconsistent results and possible recall and selection bias.

Objectives: To develop a radon exposure model and to predict domestic radon exposure for children in Switzerland. To investigate if an elevated indoor radon concentration increases risk of childhood cancers, specifically leukaemia and central nervous system (CNS) tumours.

Methods: A prospective census-based cohort design is used to investigate the association between radon exposure and childhood cancer. All children aged 0-15 years, born before

5 December 2000 (date of census), and resident in Switzerland were included in the cohort. Follow-up period lasted until death, emigration or 31 December 2008. The SCCR identified eligible cases. About 1,000 childhood cancer cases, including 285 leukaemias (227 with ALL) and 258 CNS-tumours were included. The Swiss National Cohort (SNC) provided place of residence on the date of census for all children of the cohort, mortality, emigration data for the calculation of follow-up time, and information about confounders such as socio-economic status or number of children in the household. The data was analysed using Cox regression adjusting for confounders. To assess individual exposure to radon at the place of residency, we developed a model for domestic radon exposure using the radon database of the Swiss Federal Office of Public Health and geographically referenced information (e.g. building register, geology). The radon database consists of indoor measurements for about 100,000 buildings in Switzerland. We used 44,631 measurements collected between 1994 and 2004 for model development (80% of the data) and for model validation (20%).

Rationale and significance: Selection bias will be minimal because direct contact with study participants is unnecessary. Thus, this study overcomes major methodological problems found in most previous studies on the topic and will help to reveal whether low dose ionizing radiation is associated with a higher risk for childhood cancer. The study will also provide new information on the exposure of the Swiss population to radon which is preventable but accounts for almost half of the average annual ionizing radiation dose in Switzerland.

Current status of project: We developed the radon prediction model and assessed individual exposure to radon at the place of residency using this model. We analysed if radon exposure is associated with a higher risk of childhood malignancy using Cox regression models. We did not find an association between radon exposure and childhood cancer in general, and childhood leukaemia and CNS tumours in particular.

Applicants: Röösli M. Swiss Tropical and Public Health Institute Basel; Kuehni CE. Institute of Social and Preventive Medicine, University of Bern; Huss A. Institute for Risk Assessment Sciences, Utrecht University, The Netherlands.

Project team: Hauri D, Röösli M. Swiss Tropical and Public Health Institute Basel; Kuehni CE. Institute of Social and Preventive Medicine, University of Bern; Zimmermann F. University Hospital Basel.

Funding: Swiss National Science Foundation (ProDoc Grant No PDFMP3_124951).

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Publications (published):

Hauri DD, Huss A, Zimmermann F, Kuehni CE, Röösli M. A prediction model for assessing residential radon concentration in Switzerland, *Journal of Environmental Radioactivity 2012*; 112: 83-89.

Publications (submitted):

Hauri DD, Huss A, Zimmermann F, Kuehni CE, Röösli M. Nationwide prediction of residential radon exposure of the whole Swiss population: comparison of model-based with measurement based predictions.

4.9 Effectiveness of transition from paediatric to adult care after childhood cancer

Background: Transition from paediatric to adult care is a crucial step in many chronic diseases of childhood. Treatments in paediatric oncology have improved over the past decades; now about 80% of patients survive to adulthood. However, 60% suffer from adverse somatic or psychosocial late effects from the cancer and its treatments and necessitate long-term follow-up. Generally, follow-up is well organised during the first 5-10 years after diagnosis. Often follow-up occurs in the context of a clinical trial. However, transfer of patients to adult care often fails and survivors may be lost to follow-up or continue to visit their paediatric institution despite their adult status and changing needs.

Objectives: The project aims to: 1) determine the frequency of follow-up in childhood cancer survivors when they are in paediatric care; 2) describe transfer modalities; 3) describe the health care providers involved in follow-up and transfer; 4) determine factors associated with successful transfer; and 5) describe advantages and disadvantages of different kinds of follow-up to survivors, families and health care providers from paediatric and adult wards.

Method: This study will analyse information collected from medical records on follow-up care, transitional care and transfer to adult care. Additional information on current follow-up, socio-economic characteristics and late effects comes from two separate, on-going questionnaire studies (Swiss Childhood Cancer Survivor Study and Childhood Cancer Follow-Up Study).

Rationale and Significance: The available information will be used to develop the first national guidelines for the transition of childhood cancer survivors. In addition, results will provide a basis for improvement of transitional care for other chronic diseases.

Current status of project: In the first pilot phase, begun in the second half of 2011, we checked medical records to see what information was available and what formats were used for archiving the records. Since February 2012 we collected data in six of the nine SPOG clinics. Data collection will also be a main focus in 2013.

Applicants: Michel G, Kuehni CE. Institute of Social and Preventive Medicine, University of Bern; von der Weid NX. Paediatric Oncology, University Children's Hospital Basel (UKBB); Bergsträsser E. Paediatric Oncology, University Children's Hospital Zurich; Ketterer N. Paediatric Oncology, CHUV Lausanne.

Project team: Gianinazzi ME, Michel G, Kuehni CE, Essig S, Rupp E, Brunner I, Wittwer S. Institute of Social and Preventive Medicine, University of Bern. Von der Weid NX. Paediatric Oncology, University Children's Hospital Basel (UKBB). Bergstraesser E. Paediatric Oncology, University Children's Hospital Zürich.

Funding: Swiss Cancer League (Grant No KLS 02631-08-2010).

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Publications: Expected for 2013-2014.

4.10 Mortality and second primary cancers after cancer in childhood and adolescence

Background: Despite improved cure rates, all-cause mortality of childhood cancer survivors is several times higher than in the general population. In the first 10 years after diagnosis recurrence of the primary cancer is the main cause of death, but thereafter deaths from second primary cancers predominate. This underlines the need to identify avoidable risk factors for these late consequences.

Objectives: We aim to analyse incidence and risk factors in survivors of childhood and adolescent cancer for: 1) total and cause-specific mortality, including late mortality (>5 years after diagnosis of cancer) and 2) second primary cancers.

Methods: The study population for this project consists of all children and adolescents registered in the Swiss Childhood Cancer Registry (SCCR). For all participants vital status and date of death has been updated via municipal population registers. Cause of death is obtained via linkage with the Swiss mortality statistics. Incidence of second primary cancers will be assessed via: 1) direct notification from treatment centres; 2) mortality records (for deceased); 3) data linkage with cantonal cancer registries and, 4) a questionnaire survey among all survivors. Second primary cancers reported in the questionnaire will be validated with medical records. In a first analysis we will calculate standardised mortality ratios and absolute excess risk of death in the study population compared to expected numbers in the general population. Further, we will determine risk factors for total and late mortality and for second primary cancers.

Rationale and significance: This project will provide the first data on long-term mortality and second primary cancers after cancer in childhood and adolescence in Switzerland. The identification of avoidable risk factors for premature death and second primary cancers will allow adapting treatment in new patients, aiming at maximal cure rates with minimal long-term side effects.

Current status of project: We confirmed vital status or date of death via municipal population registers, and obtained cause of death from Swiss mortality statistics. By December 2012 we identified 2196 patients who died in the first 5 years after diagnosis. Additionally, we identified 351 patients who died more than 5 years after diagnosis. Cause of death is available for 95% of patients deceased. Linkage with cantonal registries to detect second primary neoplasms is still in process.

Applicants: Kuehni CE, Michel G, Egger M, Institute of Social and Preventive Medicine (ISPM) University of Bern.

Project team: Schindler M, Kuehni CE, Michel G, Hau E, Mitter V. Institute of Social and Preventive Medicine, University of Bern, Ammann RA, University Children's Hospital, Inselspital Bern.

Funding: Swiss National Science Foundation (ProDoc Grant No PDFMP3_141775), Swiss Bridge Foundation

Contact: Claudia Kuehni (kuehni@ispm.unibe.ch)

Publications: Expected for 2014-2015.

4.11 Childhood cancer and geographically defined exposures in Switzerland: a census-based nationwide cohort study

Background: Ionising radiation is the only environmental exposure that has been clearly linked to cancer in children. It is, however, still unclear whether the dose-response relationships found in studies of persons exposed to moderate or high doses can be extrapolated to the lower doses from background radiation. In Switzerland, exposure to cosmic radiation has a relatively high variation because of differences in altitude between residential locations.

Objective: To examine the risk of cancer in children and adolescents associated with exposure to background ionising radiation from cosmic, terrestrial and artificial sources.

Methods: The study includes all children born between January 1985 and December 2008, aged 0-19 years at diagnosis and resident in Switzerland (N=5300). Analyses will be based on information obtained from the SCCR and the Swiss National Cohort (SNC), a long-term, census-based cohort that includes all Swiss inhabitants. We will compute dose rates of ionising radiation (unit: nSv/h) at address of residence at diagnosis and at birth for all cancer cases and for all individuals in the SNC aged <20 years. We will consider prenatal (conception to birth) and postnatal (birth to diagnosis) cumulative exposures. In a first analysis (aggregate data analysis), we will compare incidence rates for cancer and leukaemia across exposure categories using Poisson regression, adjusting for potential confounders. In a second step (individual data analysis) we will analyse individual time-to-event data based on record linkage between the SCCR and the SNC using Cox-proportional hazard models.

Current status of project: The study has just begun (Nov 2012-Nov 2013).

Applicants: Kuehni CE, Spycher BD. Institute of Social and Preventive Medicine, University of Bern.

Project team: Spycher BD, Lupatsch J, Kuehni CE. Institute of Social and Preventive Medicine, University of Bern.

Funding: Federal Office of Public Health (Grant No 12.008357).

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Publications: Expected for 2013-2014

4.12 The role of population mixing and exposure to infections in the aetiology of childhood leukaemia: a national cohort study

Background: Leukaemia is the most important cancer among children in industrialized countries. Infections may play a role: the incidence of acute lymphocytic leukaemia (ALL) is higher in resource-rich countries, where infections early in life are less common compared to resource-poor settings; there is a sharp peak in incidence at 2-5 years of age; local clusters of cases have been described and there is seasonal variation in the diagnosis of ALL. Kinlen proposed that population mixing, i.e. large influxes of people into previously isolated areas,

could explain clusters of childhood leukaemia. Childhood leukaemia may thus be a rare response to a common, yet unidentified, infection. Greaves proposed the delayed-immune hypothesis as an explanation for the peak incidence of ALL at 2-5 years: a lack of exposure to infections in early life could predispose the immune system to aberrant responses to subsequent 'delayed' infections.

Aims: To determine whether leukaemia (any leukaemia and ALL) diagnosed <20 years of age is associated with the following measures of population mixing at community level (Kinlen's hypothesis): 1) Volume and diversity of in-migration into communities, and 2) Change in annual in-migration; or with proxy measures of exposure to infections (Greaves' hypothesis): 3) Birth order, 4) Child density in neighbourhood, and 5) Extra-familial child-care.

Methods: The study will use data from the Swiss National Cohort (SNC), the Swiss Childhood Cancer Registry (SCCR), the childhood cancer cytogenetic database (CCD) and demographic data from the Swiss Federal Statistical Office. Primary outcomes will be any leukaemia and ALL in particular. Secondary outcomes will be the most prevalent immunophenotype, B-cell-precursor ALL, and cytogenetic subgroups like high hyperdiploidy and TEL1-AML1 translocation. Geocodes of both addresses at birth and at diagnosis will be analysed. Exposures will include percentage of population that moved into a community over 5-year periods, diversity of areas of origin (Shannon's entropy), change in annual in-migration volume relative to average in-migration in previous years, the rank of the child among all live births of the same mother, neighbourhood indices of child density developed using road network connectivity, and parental full-time employment as a proxy measure of extra-familial child-care. We will estimate and compare incidence across quintiles of exposure measures using Poisson regression (analyses of aggregated data) and Cox regression (individual data). Analyses will be adjusted for age, sex and calendar year and, in a second step, for other potential confounders.

Significance: The possibility that childhood leukaemia might be associated with a specific infection or with later exposure to infections is highly relevant for prevention. Previous studies were limited by the lack of spatial or temporal precision and few studies were able to use both residential locations at birth and at diagnosis. Many were case-control studies and at risk of selection bias and recall bias. In the present study only routine data bases with national coverage will be used and precise geocoding of both address at birth and diagnosis will allow high temporal and spatial resolution.

Current status of project: The study begins in January 2013.

Applicants: Spycher BD, Egger M and Kuehni CE, Institute of Social and Preventive Medicine, University of Bern; Ammann RA, University Children's Hospital, Inselspital Bern; Niggli F, University Children's Hospital, Zurich.

Project team: Spycher BD, Lupatsch J, Kuehni CE. Institute of Social and Preventive Medicine, University of Bern; Ammann RA, University Children's Hospital, Inselspital Bern.

Funding: Cancer Research Switzerland (Grant No KFS 3049-08-2012).

Contact: Ben Spycher (bspycher@ispm.unibe.ch)

Publications: Expected for 2014-2015

5. Publications

All articles published using SCCR data from January 2006 – December 2012 are reported below. Additional publications related to the SCCR or SPOG can be found on the SCCR and SPOG websites: www.childhoodcancerregistry.ch and www.spog.ch.

5.1 Publications in peer-reviewed journals

2013

Gianinazzi ME, Rueegg CS, Wengenroth L, Bergstraesser E, Rischewski J, Ammann RA, Kuehni CE, Michel G. Adolescent survivors of childhood cancer: are they vulnerable for psychological distress? *Psycho-Oncology 2013; doi:10.1002/pon.3249.*

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Aydin D, Feychting M, Schüz J, Röösli M. Childhood brain tumours and use of mobile phones: Comparison of a case-control study with incidence data. *Environmental Health 2012*; *11*: 35.

2011

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2009

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2008

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2007

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2006

Kuehni CE, Zwahlen M. Commentary: Numerous, heterogeneous and often poor – the studies on childhood leukaemia and socioeconomic status. *International Journal of Epidemiology 2006; 35: 384-385*

5.2 Publications in other journals

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5.3 Publications in lay journals

Kuehni CE. Krebsrisiko in der Nähe von Kernkraftwerken. *Aspect, Krebsforschung Schweiz 2012; 1:* 8-9.

Michel G. Nachsorge nach Krebs im Kindesalter- ein neues Feld für die Pflege. *Mitenand, Kinderkrebshilfe Schweiz 2012; 1: 10-11.*

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5.4 Reports

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Michel G, von der Weid NX, Adam M, Rebholz CE, Zwahlen M, Kuehni CE. The Swiss Childhood Cancer Registry. Annual Report 2005/2006. Bern: Department of Social and Preventive Medicine, University of Bern; May 2007.

Kuehni CE, Michel G, Sturdy M, Redmond S, Zwahlen M, von der Weid NX. Annual Report of the Swiss Childhood Cancer Registry 2004, Bern: Department of Social and Preventive Medicine, University of Bern; September 2005.

6. Abbreviations

ALL	Acute Lymphoblastic Leukaemia
AML	Acute Myeloid Leukaemia
CANUPIS	Childhood Cancer and Nuclear Power Plants in Switzerland
CCFU	Childhood Cancer Follow-up study
CHUV	Centre Hospitalier Universitaire Vaudois
CNS	Central Nervous System
DNA	Deoxyribonucleic Acid
ENCR	European Network of Cancer Registries
FOPH	Federal Office of Public Health
GCCR	German Childhood Cancer Registry, Mainz, Germany
GH	Growth Hormone
GHD	Growth Hormone Deficiency
GIS	Geographic Information System
HUG	Hôpitaux Universitaires de Genève
HRQoL	Health Related Quality of Life
IACR	International Association of Cancer Registries
IARC	International Agency for Research on Cancer
ICCC-3	International Classification of Childhood Cancer, Third revision
ICD-10	International Statistical Classification of Diseases and Related Health Problems, Tenth revision
ICD-O-3	International Statistical Classification of Diseases for Oncology, Third edition
IRR	Incidence Rate Ratio
ISPM	Institute of Social and Preventive Medicine, Bern
LCH	Langerhans Cell Histiocytosis
MD	Medical Doctor
MSc	Master of Science
NBR	National Birth Registry
NICER	National Institute for Cancer Epidemiology and Registration, Zurich
NPP	Nuclear Power Plants
nSv/h	Nano Sievert per Hour
PanCare	Pan-European Network for Care of Survivors after Childhood and Adolescent Cancers
PanCareSurFup	PanCare Childhood and Adolescent Cancer Survivor Care and Follow-up Studies

Abbreviations - continued

PD	Privatdozent
PhD	Doctor of Philosophy
RF	Radio Frequency
SAGhE	Safety and Appropriateness of Growth Hormone Treatment in Europe
SCCR	Swiss Childhood Cancer Registry
SCCSS	Swiss Childhood Cancer Survivor Study
SFSO	Swiss Federal Statistical Office
SNC	Swiss National Cohort
SPOG	Swiss Paediatric Oncology Group
STS	Soft Tissue Sarcoma
UKBB	Universitätskinderspital beider Basel
WHO	World Health Organization

7. Appendix: Classification of cancer diagnoses

International Classification of Childhood Cancer - ICCC-3

The third edition of the International Classification of Childhood Cancer (ICCC-3) represents the standard for presentation of international data on childhood cancer incidence and survival.[5] It applies the rules, nomenclature and codes (morphology, topography and behaviour) of the ICD-O-3. Furthermore, ICCC-3 categories are defined in conformity with international classifications of the pathology and genetics of childhood cancers. In the ICCC-3, three hierarchical levels have been developed: level one consists of 12 main diagnostic groups and level two of 47 diagnostic subgroups. These two levels of the ICCC-3 allow standardised comparison of the broad categories of childhood tumours. Level three, an optional "extended" classification, comprises two to eleven divisions of selected diagnostic subgroups. The division of some diagnostic subgroups, e.g. leukaemias and Non-Hodgkin lymphomas, reflects the availability of detailed cytogenetic or molecular information that permits homogeneous groups of tumours to be distinguished within them and thus allows their separate study. The Swiss childhood cancer registry uses level one to three. Only malignant neoplasms are classified in ICCC-3, with the exception of non-malignant intracranial and intraspinal tumours. Tumours known to occur only rarely in young patients are also included in ICCC-3. The ICCC-3 is used if data are compared with other childhood cancer registries.

International Statistical Classification of Diseases for Oncology - ICD-O-3

The third edition of the International Statistical Classification of Diseases for Oncology (ICD-O-3)[6] has been developed by a working group hosted by the International Association of Research in Cancer (IARC) and WHO. The morphology code for neoplasm has been revised, especially for lymphomas and leukaemias. In contrast to the ICD-10 classification, ICD-O-3 uses only one set of four characters for topography (based on the malignant neoplasm section of ICD-10). The topography code remains the same for all neoplasms of that site. The behaviour code is incorporated as the fifth digit in the morphology field. It identifies whether the tumour is malignant, benign, of uncertain or unknown behaviour, in situ, presumed to be primary or secondary. ICD-O-3 is used to compare data with general cancer registries.

International Statistical Classification of Diseases and Related Health Problems - ICD-10

The International Statistical Classification of Diseases and Related Health Problems (ICD)[7] permits the systematic recording, analysis, interpretation and comparison of mortality and morbidity data collected in different regions and at different time periods. The ICD has become the international standard diagnostic classification for all general epidemiological purposes. The ICD-10 classification comprises three volumes: Volume 1 contains the main classifications; Volume 2 provides guidance for users of the ICD; and Volume 3 is the alphabetical index to the classification. Classification is divided into 21 chapters. The first character of the ICD code is a letter. Each letter is associated with a particular chapter, e.g. the letter D is used in both chapter II "Neoplasms" and chapter III "Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism". The topography code in Volume 3 describes the site and the behaviour of the neoplasm: malignant, secondary or metastatic, in situ, benign or of unknown behaviour. The morphology codes listed in Volume 1 are the same as those used in the special adaptation of the ICD for oncology, the ICD-O6[7].

5 Steliarova-Foucher E, Stiller C, Lacour B, Kaatsch P. International Classification of Childhood Cancer, Third Edition. Cancer 2005; 103:1457-67.

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